Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	23151	bioluminesc$ or fluorescen$ near4 protein$1 or luciferase$1 or photoprotein$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:40
L2	152305	bubble$	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:41
L3	24	1 same 2	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:35
L4	83381	toy or novelty	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:43
L5	46	1 and 2 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L6	28	1 same 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L7	40	1 and toy	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:45
L9	27	7 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L10	34	1 and novelty adj item$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:53
L11	18	10 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L12	286	((chemilumines$ or lumines$8 or glow$8) same 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:28
L13	29	((chemilumines$ or lumines$8 or glow$8) near4 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:32
L14	9	12 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:34
L15	0	12 and 2 adj bath	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:34
L16	145975	fluorescen$	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:35
L17	698	16 same 2	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:36
L18	12	17 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:49
L19	33788	(toy or novelty adj item$1)	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:55
L20	71	16 and 2 and 19	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:55
L21	9343	16 adj protein$1 or gfp	US-PGPUB; USPAT	OR	OFF	2004/01/30 14:08
L22	33	21 and 19	US-PGPUB; USPAT	OR	OFF	2004/01/30 14:08

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	23151	biolumines$ or fluorescen$ near4 protein$1 or luciferase$1 or photoprotein$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:40
L2	152305	bubble$	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:41
L3	24	1 same 2	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:42
L4	83381	toy or novelty	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:43
L5	46	1 and 2 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L6	28	1 same 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L7	40	1 and toy	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:45
L9	27	7 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L10	34	1 and novelty adj item$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 12:00
L11	18	10 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00

PGPUB-DOCUMENT-NUMBER: 20040019132

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040019132 A1

TITLE: Bone graft substitutes

PUBLICATION-DATE: January 29, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Long, Marc	Memphis	TN	US	
Cooper, Michael B.	Memphis	TN	US	
Kinnane, Keith M.	Bartlett	TN	US	
Allen, Trevor	York	TN	GB	
Schryver, Jeffrey E.	Cordova		US	

APPL-NO: 10/ 621633

DATE FILED: July 17, 2003

RELATED-US-APPL-DATA:

child 10621633 A1 20030717

parent division-of 09792681 20010223 US GRANTED

parent-patent 6630153 US

US-CL-CURRENT: 523/115, 623/23.5

ABSTRACT:

The present invention is directed to methods and compositions for manufacturing a bone graft substitute. A powder compaction process is utilized to generate a shaped product comprised of a granulated bone material, such as demineralized bone matrix. In addition, a processing aid is utilized to facilitate compaction of the granulated bone material and for release of the product from the die.

[0001] The present invention claims priority to U.S. patent application Ser. No. 09/792,681, filed Feb. 23, 2001, which is incorporated by reference herein in its entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (14):
[0056] The term "JAX.TM." as used herein is defined as a bone graft substitute particle which generally has the shape of a toy jack. In a specific embodiment, it is a three-dimensional six-armed star shape.

Detail Description Paragraph - DETX (31):
[0073] In a specific embodiment, the bone material of the present invention

is colored to make it more visible. In another specific embodiment, differently shaped BGS of the present invention are denoted with different colors for better differentiation of the particles. In another specific embodiment, the particles are coated or have contained within them an agent such as green fluorescent protein or blue fluorescent protein to make them fluorescent and therefore more visible.

PGPUB-DOCUMENT-NUMBER: 20040018976

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040018976 A1

TITLE: Polynucleotide encoding novel human G-protein coupled receptors, and splice variants thereof

PUBLICATION-DATE: January 29, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Feder, John N.	Belle Mead	NJ	US	
Mintier, Gabriel	Hightstown	NJ	US	
Ramanathan, Chandra S.	Wallingford	CT	US	

APPL-NO: 10/ 436715

DATE FILED: May 13, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60380336 20020514 US

US-CL-CURRENT: 514/12, 435/320.1 , 435/325 , 435/69.1 , 530/350 , 530/388.22 , 536/23.2

ABSTRACT:

The present invention provides novel polynucleotides encoding HGPRBMY30_1, HGPRBMY30_2, HGPRBMY30_3, HGPRBMY41_1, HGPRBMY41_2, HGPRBMY41_3, HGPRBMY42, HGPRBMY42_1, HGPRBMY43, and/or HGPRBMY44 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel HGPRBMY30_1, HGPRBMY30_2, HGPRBMY30_3, HGPRBMY41_1, HGPRBMY41_2 HGPRBMY41_3, HGPRBMY42, HGPRBMY42_1, HGPRBMY43, and/or HGPRBMY44 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

[0001] This application claims benefit to provisional application U.S. Serial No. 60/380,336 filed May 14, 2002, under 35 U.S.C. 119(e). The entire teachings of the referenced applications are incorporated herein by reference.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (15):

[0014] Although olfactory receptors are typically associated with olfactory function and tend to localize to the olfactory bulb, there is increasing evidence that olfactory receptors and olfactory-like receptors may play more diverse roles in varying tissues (Yuan, T, T., Toy, P., McClary, J. A., Lin, R, J., Miyamoto, N, G., Kretschmer, P, J. Gene., 278(1-2):41-51, (2001); Blache,

P., Gros, L., Salazar, G., Bataille, D, Biochem, Biophys, Res, Commun., 242(3):669-72, (1998); and Matsuoka, I., Mori, T., Aoki, J., Sato, T., Kurihara, K, Biochem, Biophys, Res, Commun., 194(I):504-11, (1993)).

Detail Description Paragraph - DETX (711):

[0824] The present invention further encompasses antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent. The antibodies can be used diagnostically to, for example, monitor the development or progression of a tumor as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions. The detectable substance may be coupled or conjugated either directly to the antibody (or fragment thereof) or indirectly, through an intermediate (such as, for example, a linker known in the art) using techniques known in the art. See, for example, U.S. Pat. No. 4,741,900 for metal ions which can be conjugated to antibodies for use as diagnostics according to the present invention. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include 125I, 131I, 111In or 99Tc.

Detail Description Paragraph - DETX (725):

[0838] Various diagnostic assay techniques are known in the art, such as competitive binding assays, direct or indirect sandwich assays and immunoprecipitation assays conducted in either heterogeneous or homogenous phases (Zola, Monoclonal Antibodies: A Manual of Techniques, CRC Press, Inc., (1987), pp147-158). The antibodies used in the diagnostic assays can be labeled with a detectable moiety. The detectable moiety should be capable of producing, either directly or indirectly, a detectable signal. For example, the detectable moiety may be a radioisotope, such as 2H, 14C, 32P, or 125I, a florescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase, green fluorescent protein, or horseradish peroxidase. Any method known in the art for conjugating the antibody to the detectable moiety may be employed, including those methods described by Hunter et al., Nature, 144:945 (1962); Dafvid et al., Biochem., 13:1014 (1974); Pain et al., J. Immunol. Metho., 40:219(1981); and Nygren, J. Histochem. And Cytochem., 30:407 (1982).

Detail Description Paragraph - DETX (731):

[0844] The antibodies of the invention may be assayed for immunospecific binding by any method known in the art. The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few.

Such assays are routine and well known in the art (see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, which is incorporated by reference herein in its entirety). Exemplary immunoassays are described briefly below (but are not intended by way of limitation).

Detail Description Paragraph - DETX (1273):

[1370] 5. George, S. E., Bungay, B. J., and Naylor, L. H.: Functional coupling of endogenous serotonin (5-HT1B) and calcitonin (C1a) receptors in Cho cells to a cyclic AMP-responsive luciferase reporter gene. J. Neurochem. 1997; 69: 1278-1285.

Detail Description Paragraph - DETX (1296):

[1389] The physiological function of the HGPRBMY30.sub.--1, HGPRBMY30.sub.--2, HGPRBMY30.sub.--3, HGPRBMY41.sub.--1, HGPRBMY41.sub.--2, HGPRBMY41.sub.--3, HGPRBMY42, HGPRBMY42.sub.--1, HGPRBMY43, and/or HGPRBMY44 polypeptide may be assessed by expressing the sequences encoding HGPRBMY30.sub.--1, HGPRBMY30.sub.--2, HGPRBMY30.sub.--3, HGPRBMY41.sub.--1, HGPRBMY41.sub.--2, HGPRBMY41.sub.--3, HGPRBMY42, HGPRBMY42.sub.--1, HGPRBMY43, and/or HGPRBMY44 at physiologically elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression vector containing a strong promoter that drives high levels of cDNA expression (examples are provided elsewhere herein). Vectors of choice include pCMV SPORT (Life Technologies) and pCR3.1 (Invitrogen, Carlsbad Calif.), both of which contain the cytomegalovirus promoter. 5-10, ug of recombinant vector are transiently transfected into a human cell line, preferably of endothelial or hematopoietic origin, using either liposome formulations or electroporation. 1-2 ug of an additional plasmid containing sequences encoding a marker protein are cotransfected. Expression of a marker protein provides a means to distinguish transfected cells from nontransfected cells and is a reliable predictor of cDNA expression from the recombinant vector. Marker proteins of choice include, e.g., Green Fluorescent Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser optics-based technique, is used to identify transfected cells expressing GFP or CD64-GFP and to evaluate the apoptotic state of the cells and other cellular properties. FCM detects and quantifies the uptake of fluorescent molecules that diagnose events preceding or coincident with cell death. These events include changes in nuclear DNA content as measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; down-regulation of DNA synthesis as measured by decrease in bromodeoxyuridine uptake; alterations in expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies; and alterations in plasma membrane composition as measured by the binding of fluorescein-conjugated Annexin V protein to the cell surface. Methods in flow cytometry are discussed in Ormerod, M. G. (1994) Flow Cytometry, Oxford, New York N.Y.

Detail Description Paragraph - DETX (1328):

[1411] Another screening procedure involves use of mammalian cells (CHO, HEK293, Xenopus Oocytes, RBL-2H3, etc.) which are transfected to express the receptor of interest, and which are also transfected with a reporter gene construct that is coupled to activation of the receptor (for example, luciferase or beta-galactosidase behind an appropriate promoter). The cells are contacted with a test substance and the receptor agonist (ligand), such as LPA, and the signal produced by the reporter gene is measured after a defined period of time. The signal can be measured using a luminometer,

spectrophotometer, fluorimeter, or other such instrument appropriate for the specific reporter construct used. Change of the signal generated by the ligand indicates that a compound is a potential antagonist or agonist for the receptor.

Detail Description Paragraph - DETX (1621):

[1648] In yet another screening procedure, mammalian cells are transfected to express the receptor of interest, and are also transfected with a reporter gene construct that is coupled to activation of the receptor (for example, but not limited to luciferase or beta-galactosidase behind an appropriate promoter). The cells are contacted with a test substance and the receptor agonist (ligand), such as dATP, dAMP, or UTP, and the signal produced by the reporter gene is measured after a defined period of time. The signal can be measured using a luminometer, spectrophotometer, fluorimeter, or other such instrument appropriate for the specific reporter construct used. Inhibition of the signal generated by the ligand indicates that a compound is a potential antagonist for the receptor.

PGPUB-DOCUMENT-NUMBER: 20030232359

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030232359 A1

TITLE: Polynucleotide encoding a novel human G-protein coupled receptor, HGPRBMY40_2

PUBLICATION-DATE: December 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ramanathan, Chandra S.	Wallingford	CT	US	
Mintier, Gabriel	Hightstown	NJ	US	
Gopal, Shuba	New York	NY	US	
Feder, John N.	Belle Mead	NJ	US	

APPL-NO: 10/ 391634

DATE FILED: March 18, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60365350 20020318 US

US-CL-CURRENT: 435/6, 435/226 , 435/320.1 , 435/325 , 435/69.1 , 536/23.2

ABSTRACT:

The present invention provides novel polynucleotides encoding HGPRBMY40_2 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel HGPRBMY40_2 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

[0001] This application is a continuation-in-part application of provisional application U.S. Serial No. 60/365,350 filed Mar. 18, 2002, and claims benefit of the same under 35 U.S.C. 119(e). The entire teachings of the referenced applications are incorporated herein by reference.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (15):

[0014] Although olfactory receptors are typically associated with olfactory function and tend to localize to the olfactory bulb, there is increasing evidence that olfactory receptors and olfactory-like receptors may play more diverse roles in varying tissues (Yuan, T, T., Toy, P., McClary, J. A., Lin, R, J., Miyamoto, N, G., Kretschmer, P, J. Gene., 278(1-2):41-51, (2001); Blache, P., Gros, L., Salazar, G., Bataille, D, Biochem, Biophys, Res, Commun., 242(3):669-72, (1998); and Matsuoka, I., Mori, T., Aoki, J., Sato, T.,

Kurihara, K, Biochem, Biophys, Res, Commun., 194(I):504-11, (1993)).

Detail Description Paragraph - DETX (105):

[0187] Another screening procedure involves use of mammalian cells (CHO, HEK293, Xenopus Oocytes, RBL-2H3, etc.) which are transfected to express the receptor of interest, and which are also transfected with a reporter gene construct that is coupled to activation of the receptor (for example, luciferase or beta-galactosidase behind an appropriate promoter). The cells are contacted with a test substance and the receptor agonist (ligand), such as LPA, and the signal produced by the reporter gene is measured after a defined period of time. The signal can be measured using a luminometer, spectrophotometer, fluorimeter, or other such instrument appropriate for the specific reporter construct used. Change of the signal generated by the ligand indicates that a compound is a potential antagonist or agonist for the receptor.

Detail Description Paragraph - DETX (257):

[0339] The present invention further encompasses antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent. The antibodies can be used diagnostically to, for example, monitor the development or progression of a tumor as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions. The detectable substance may be coupled or conjugated either directly to the antibody (or fragment thereof) or indirectly, through an intermediate (such as, for example, a linker known in the art) using techniques known in the art. See, for example, U.S. Pat. No. 4,741,900 for metal ions which can be conjugated to antibodies for use as diagnostics according to the present invention. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include 125I, 131I, 111In or 99Tc.

Detail Description Paragraph - DETX (271):

[0353] Various diagnostic assay techniques are known in the art, such as competitive binding assays, direct or indirect sandwich assays and immunoprecipitation assays conducted in either heterogeneous or homogenous phases (Zola, Monoclonal Antibodies: A Manual of Techniques, CRC Press, Inc., (1987), ppl47-158). The antibodies used in the diagnostic assays can be labeled with a detectable moiety. The detectable moiety should be capable of producing, either directly or indirectly, a detectable signal. For example, the detectable moiety may be a radioisotope, such as 2H, 14C, 32P, or 125I, a florescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase, green fluorescent protein, or horseradish peroxidase. Any method known in the art for conjugating the antibody to the detectable moiety may be employed, including those methods described by Hunter et al., Nature, 144:945 (1962); David et al., Biochem., 13:1014 (1974); Pain et al., J.

Immunol. Metho., 40:219(1981); and Nygren, J. Histochem. And Cytochem., 30:407 (1982).

Detail Description Paragraph - DETX (277):

[0359] The antibodies of the invention may be assayed for immunospecific binding by any method known in the art. The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few. Such assays are routine and well known in the art (see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, which is incorporated by reference herein in its entirety). Exemplary immunoassays are described briefly below (but are not intended by way of limitation).

Detail Description Paragraph - DETX (830):

[0904] The physiological function of the HGPRBMY40.sub.--2 polypeptide may be assessed by expressing the sequences encoding HGPRBMY40.sub.--2 at physiologically elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression vector containing a strong promoter that drives high levels of cDNA expression (examples are provided elsewhere herein). Vectors of choice include pCMV SPORT (Life Technologies) and pCR3.1 (Invitrogen, Carlsbad Calif.), both of which contain the cytomegalovirus promoter. 5-10, ug of recombinant vector are transiently transfected into a human cell line, preferably of endothelial or hematopoietic origin, using either liposome formulations or electroporation. 1-2 ug of an additional plasmid containing sequences encoding a marker protein are cotransfected. Expression of a marker protein provides a means to distinguish transfected cells from nontransfected cells and is a reliable predictor of cDNA expression from the recombinant vector. Marker proteins of choice include, e.g., Green Fluorescent Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser optics-based technique, is used to identify transfected cells expressing GFP or CD64-GFP and to evaluate the apoptotic state of the cells and other cellular properties. FCM detects and quantifies the uptake of fluorescent molecules that diagnose events preceding or coincident with cell death. These events include changes in nuclear DNA content as measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; down-regulation of DNA synthesis as measured by decrease in bromodeoxyuridine uptake; alterations in expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies; and alterations in plasma membrane composition as measured by the binding of fluorescein-conjugated Annexin V protein to the cell surface. Methods in flow cytometry are discussed in Ormerod, M. G. (1994) Flow Cytometry, Oxford, New York N.Y.

Detail Description Paragraph - DETX (874):

[0941] Another screening procedure involves use of mammalian cells (CHO, HEK293, Xenopus Oocytes, RBL-2H3, etc.) which are transfected to express the receptor of interest, and which are also transfected with a reporter gene construct that is coupled to activation of the receptor (for example, luciferase or beta-galactosidase behind an appropriate promoter). The cells are contacted with a test substance and the receptor agonist (ligand), such as

LPA, and the signal produced by the reporter gene is measured after a defined period of time. The signal can be measured using a luminometer, spectrophotometer, fluorimeter, or other such instrument appropriate for the specific reporter construct used. Change of the signal generated by the ligand indicates that a compound is a potential antagonist or agonist for the receptor.

Detail Description Paragraph - DETX (1155):

[1196] In yet another screening procedure, mammalian cells are transfected to express the receptor of interest, and are also transfected with a reporter gene construct that is coupled to activation of the receptor (for example, but not limited to luciferase or beta-galactosidase behind an appropriate promoter). The cells are contacted with a test substance and the receptor agonist (ligand), such as dATP, dAMP, or UTP, and the signal produced by the reporter gene is measured after a defined period of time. The signal can be measured using a luminometer, spectrophotometer, fluorimeter, or other such instrument appropriate for the specific reporter construct used. Inhibition of the signal generated by the ligand indicates that a compound is a potential antagonist for the receptor.

PGPUB-DOCUMENT-NUMBER: 20030198640

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030198640 A1

TITLE: Methods and compositions for treating inflammatory bowel diseases relating to human tumor necrosis factor-gamma-beta

PUBLICATION-DATE: October 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Yu, Guo-Liang	Berkeley	CA	US	
Ni, Jian	Germantown	MD	US	
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Zhang, Jun	San Diego	CA	US	
Wei, Ping	Brookeville	MD	US	

APPL-NO: 10/ 310793

DATE FILED: December 6, 2002

RELATED-US-APPL-DATA:

child 10310793 A1 20021206

parent continuation-in-part-of 10226294 20020823 US PENDING

child 10310793 A1 20021206

parent continuation-in-part-of 09899059 20010706 US PENDING

child 10310793 A1 20021206

parent continuation-in-part-of 09559290 20000427 US ABANDONED

child 10310793 A1 20021206

parent continuation-in-part-of 09246129 19990208 US PENDING

child 10310793 A1 20021206

parent continuation-in-part-of 09131237 19980807 US PENDING

child 10310793 A1 20021206

parent continuation-in-part-of 09005020 19980109 US ABANDONED

child 10310793 A1 20021206

parent continuation-in-part-of 08461246 19950605 US ABANDONED

child 10310793 A1 20021206

parent continuation-in-part-of PCT/US94/12880 19941107 US PENDING

non-provisional-of-provisional 60336695 20011207 US

non-provisional-of-provisional 60314381 20010824 US

non-provisional-of-provisional 60278449 20010326 US

non-provisional-of-provisional 60216879 20000707 US

non-provisional-of-provisional 60180908 20000208 US

non-provisional-of-provisional 60134067 19990513 US

non-provisional-of-provisional 60132227 19990503 US

non-provisional-of-provisional 60131963 19990430 US

non-provisional-of-provisional 60074047 19980209 US

US-CL-CURRENT: 424/145.1

ABSTRACT:

The present invention encompasses methods for detection, diagnosis, prevention, treatment, and/or amelioration of inflammatory bowel diseases and disorders using TNF-gamma-.beta. and its receptors DR3 and TR6. In particular the invention encompasses methods of using TNF-gamma-.beta., DR3 and TR6 polypeptides, as well as antibodies, and antagonists thereto, in the diagnosis, prognosis and treatment of ulcerative colitis and/or Crohn's disease. Methods of screening for antagonists of the TNF-gamma-.beta. polypeptide, together with therapeutic uses of such antagonists are also disclosed.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application, which claims benefit under 35 U.S.C. .sctn.119(e) of U.S. Provisional Application No. 60/336,695, filed Dec. 7, 2001; is a Continuation-In-Part of U.S. patent application Ser. No. 10/226,294, filed Aug. 23, 2002; which in turn claims the benefit of priority under 35 U.S.C. .sctn.119(e) based on U.S. Provisional Application No. 60/314,381, filed Aug. 24, 2001, and is a Continuation-In-Part of U.S. patent application Ser. No. 09/899,059, filed Jul. 6, 2001; which in turn claims the benefit of priority under 35 U.S.C. .sctn.119(e) based on U.S. Provisional Application Nos. 60/278,449 and 60/216,879, filed Mar. 26, 2001 and Jul. 7, 2000 respectively, and is a Continuation-In-Part of U.S. patent application Ser. No. 09/559,290, filed Apr. 27, 2000; which in turn claims the benefit of priority under 35 U.S.C. .sctn.119(e) based on U.S. Provisional Application Nos. 60/180,908, 60/134,067, 60/132,227 and 60/131,963, filed Feb. 8, 2000, May 13, 1999, May 3, 1999 and Apr. 30, 1999 respectively, and is a Continuation-In-Part of U.S. patent application Ser. No. 09/246,129, filed Feb. 8, 1999; which in turn claims the benefit of priority under 35 U.S.C. .sctn.119(e) based on U.S. Provisional Application No. 60/074,047, filed Feb. 9, 1998, and is a Continuation-In-Part of U.S. patent application Ser. No. 09/131,237, filed Aug. 7, 1998; which in turn is a Continuation-In-Part of U.S. patent application Ser. No. 09/005,020, filed Jan. 9, 1998, now abandoned; which in turn is a Continuation-In-Part of U.S. patent application Ser. No. 08/461,246, filed Jun. 5, 1995, now abandoned; which in turn is a Continuation-In-Part of PCT/US94/12880 filed Nov. 7, 1994. The contents of each of the above-identified applications and their associated sequence listings are hereby incorporated by reference in their entireties.

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Detail Description Paragraph - DETX (116):

[0222] Moreover, the present invention further provides polypeptides having one or more residues deleted from the carboxy terminus of the amino acid sequence of the polypeptide shown in SEQ ID NO:2 (FIGS. 1A-1B). For example, the present invention provides polypeptides comprising, or alternatively consisting of, the amino acid sequence of residues 1-m.sup.1 of the amino acid sequence in SEQ ID NO:2, where ml is any integer in the range 6-250. More in particular, in certain embodiments, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group consisting of residues M-1 to L-250; M-1 to F-249; M-1 toA-248; M-1 to G-247; M-1 to F-246; M-1 toF-245; M-1 to T-244; M-1 to K-243; M-1 toD-242; M-1 to E-241; M-1 to K-240; M-1 toT-239; M-1 to Y-238; M-1 to D-237; M-1 toV-236; M-1 to L-235; M-1 to S-234; M-1 toL-233; M-1 to D-232; M-1 to S-231; M-1 toV-230; M-1 to N-229; M-1 to V-228; M-1 toM-227; M-1 to L-226; M-1 to K-225; M-1 toD-224; M-1 to G-223; M-1 to E-222; M-1 toQ-221; M-1 to L-220; M-1 to S-219; M-1 toF-218; M-1 to M-217; M-1 to A-216; M-1 toG-215; M-1 to L-214; M-1 to Y-213; M-1 toI-212; M-I to P-211; M-I to Q-210; M-I toF-209; M-1 to W-208; M-1 to N-207; M-1 toS-206; M-1 to G-205; M-1 to V-204; M-1 toE-203; M-1 to C-202; M-1 to V-201; M-1 toS-200; M-1 to K-199; M-1 to T-198; M-1 toG-197; M-1 to M-196; M-1 to L-195; M-1 toL-194; M-1 to Q-193; M-1 to T-192; M-1 toP-191; M-1 to E-190; M-1 to P-189; M-1 toY-188; M-1 to S-187; M-1 to D-186; M-1 toT-185; M-1 to V-184; M-1 to K-183; M-1 toT-182; M-1 to 1-181; M-1 to V-180; M-1 toV-179; M-1 to T-178; M-1 to 1-177; M-1 toS-176; M-1 to D-175; M-1 to P-174; M-1 toK-173; M-1 to N-172; M-1 to P-171; M-1 toR-170; M-1 to G-169; M-1 to A-168; M-1 toQ-167; M-1 to R-166; M-1 to 1-165; M-1 toE-164; M-1 to S-163; M-1 to C-162; M-1 toE-161; M-1 to S-160; M-1 to T-159; M-1 toM-158; M-1 to G-157; M-1 to R-156; M-1 toF-155; M-1 to T-154; M-1 to V-153; M-1 toQ-152; M-1 to S-151; M-1 to Y-150; M-1 toL-149; M-1 to F-148; M-1 to Y-147; M-1 toD-146; M-1to G-145; M-1 to S-144; M-1 toE-143; M-1 to P-142; M-1 to 1-141; M-1 toL-140; M-1 to L-139; M-1 to F-138; M-1 toK-137; M-1 to N-136; M-1 to T-135; M-1 toY-134; M-1 to N-133; M-1 to M-132; M-1 toR-131; M-1 to N-130; M-1 to K-129; M-1 toT-128; M-1 to F-127; M-1 to A-126; M-1 toL-125; M-1 to G-124; M-1 to L-123; M-1 toE-122; M-1 to H-121; M-1 to E-120; M-1 toW-119; M-1 to H-118; M-1 to L-117; M-1 toA-116; M-1 to P-115; M-1 to F-I 14; M-1 toQ-113; M-1 to N-112; M-1 to K-111; M-1 toF-110; M-1 to H-109; M-1 to Q-108; M-1 toT-107; M-1 to P-106; M-1 to T-105; M-1 toQ-104; M-1 to R-103; M-1 to V-102; M-1 toV-101; M-1 to T-100; M-1 to L-99; M-1 to H-98;M-1 to A-97; M-1 to R-96; M-1 to P-95; M-1 toK-94; M-1.to D-93; M-1 to G-92; M-1 to D-91;M-1 to A-90; M-1 to R-89; M-1 to L-88; M-1 toP-87; M-1 to A-86; M-1 to Y-85; M-1 to V-84;M-1 to Q-83; M-1 to Q-82; M-1 to H-81; M-1 toS-80; M-1 to P-79; M-1 to A-78; M-1 to F-77;M-1 to E-76; M-1 to Q-75; M-1 to G-74; M-1 toK-73; M-1 to L-72; M-1 to A-71; M-1 to Q-70;M-1 to F-69; M-1 to Q-68; M-1 to V-67; M-1 toC-66; M-1 to A-65; M-1 to E-64; M-1 to G-63;M-1 to Q-62; M-1 to A-61; M-1 to R-60; M-1 toL-59; M-1 to Q-58; M-1 to S-57; M-1 to V-56;M-1 to L-55; M-1 to L-54; M-1 to Y-53; M-1 toT-52; M-1 to T-51; M-1 to L-50; M-1 to G-49;M-1 to A-48; M-1 to L-47; M-1 to F-46; M-1 toP-45; M-1 to L-44; M-1 to L-43; M-1 to V-42;M-1 to L-41; M-1 to C-40; M-1 to C-39; M-1 toT-38; M-1 to L-37; M-1 to A-36; M-1 to W-35;M-1 to R-34; M-1 to A-33; M-1 to S-32; M-1 toS-31; M-1 to S-30; M-1 to R-29; M-1 to A-28;M-1 to K-27; M-1 to P-26; M-1 to R-25; M-1 toC-24; M-1 to S-23; M-1 to G-22; M-1 to H-21;M-1 to E-20; M-1 to P-19; M-1 to L-18; M-1 toM-17; M-1 to E-16; M-1 to V-15; M-1 to S-14;M-1 to A-13; M-1 to T-12; M-1 to E-11; M-1 toG-10; M-1 to F-9; M-1 to S-8; M-1 to L-7; M-1 to G-6; of SEQ ID NO:2. Polynucleotides encoding the above polypeptide fragments and antibodies that bind the above polypeptide fragments are also encompassed by the invention.

Detail Description Paragraph - DETX (118):

[0224] The invention also provides polypeptides having one or more amino acids deleted from both the amino and the carboxyl termini of the polypeptide of SEQ ID NO:2 (FIGS. 1A-1B). For example, amino terminal and carboxyl terminal deletions of the polypeptide sequence may be described generally, for example, as having residues n.sup.1-m.sup.1 of SEQ ID NO:2 where n.sup.1 is an integer in the range of 1-237 and m.sup.1 is an integer in the range of 16-251. For example, and more in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group consisting of residues of M-1 to V-15; A-2 to E-16; E-3 to M-17; D-4 toL-18; L-5 to P-19; G-6 to E-20; L-7 to H-21; S-8 to G-22; F-9 to S-23; G-10 to C-24; E-11 toR-25; T-12 to P-26; A-13 to K-27; S-14 to A-28;V-15 to R-29; E-16 to S-30; M-17 to S-31; L-18 to S-32; P-19 to A-33; E-20 to R-34; H-21 toW-35; G-22 to A-36; S-23 to L-37; C-24 to T-38;R-25 to C-39; P-26 to C-40; K-27 to L-41; A-28 to V-42; R-29 to L-43; S-30 to L-44; S-31 toP-45; S-32 to F-46; A-33 to L-47; R-34 to A-48;W-35 to G-49; A-36 to L-50; L-37 to T-51; T-38 to T-52; C-39 to Y-53; C-40 to L-54; L-41 toL-55; V-42 to V-56; L-43 to S-57; L-44 to Q-58;P-45 to L-59; F-46 to R-60; L-47 to A-61; A-48 to Q-62; G-49 to G-63; L-50 to E-64; T-51 toA-65; T-52 to C-66; Y-53 to V-67; L-54 to Q-68;L-55 to F-69; V-56 to Q-70; S-57 to A-71; Q-58 to L-72; L-59 to K-73; R-60 to G-74; A-61 toQ-75; Q-62 to E-76; G-63 to F-77; E-64 to A-78;A-65 to P-79; C-66 to S-80; V-67 to H-81; Q-68 to Q-82; F-69 to Q-83; Q-70 to V-84; A-71 toY-85; L-72 to A-86; K-73 to P-87; G-74 to L-88;Q-75 to R-89; E-76 to A-90; F-77 to D-91; A-78 to G-92; P-79 to D-93; S-80 to K-94; H-81 toP-95; Q-82 to R-96; Q-83 to A-97; V-84 to H-98;Y-85 to L-99; A-86 to T-100; P-87 to V-101; L-88 to V-102; R-89 to R-103; A-90 to Q-104;D-91 to T-105; G-92 to P-106; D-93 to T-107;K-94 to Q-108; P-95 to H-109; R-96 to F-110; A-97 to K-111; H-98 to N-112; L-99 to Q-113;T-100 to F-114; V-101 to P-115; V-102 toA-116; R-103 to L-117; Q-104 to H-118; T-105 to W-119; P-106 to E-120; T-107 to H-121;Q-108 to E-122; H-109 to L-123; F-110 toG-124; K-111 to L-125; N-112 to A-126; Q-113 to F-127; F-114 to T-128; P-115 to K-129;A-116 to N-130; L-117 to R-131; H-118 toM-132; W-119 to N-133; E-120 to Y-134; H-121 to T-135; E-122 to N-136; L-123 to K-137;G-124 to F-138; L-125 to L-139; A-126 to L-140;F-127 to 1-141; T-128 to P-142; K-129 to E-143;N-130 to S-144; R-131 to G-145; M-132 toD-146; N-133 to Y-147; Y-134 to F-148; T-135 to 1-149; N-136 to Y-150; K-137 to S-151; F-138 to Q-152; L-139 to V-153; L-140 to T-154; I-141 to F-155; P-142 to R-156; E-143 to G-157; S-144 to M-158; G-145 to T-159; D-146 to S-160;Y-147 to E-161; F-148 to C-162; 1-149 to S-163;Y-150 to E-164; S-151 to 1-165; Q-152 to R-166;V-153 to Q-167; T-154 to A-168; F-155 toG-169; R-156 to R-170; G-157 to P-171; M-158 to N-172; T-159 to K-173; S-160 to P-174;E-161 to D-175; C-162 to S-176; S-163 to I-177;E-164 to T-178; 1-165 to V-179; R-166 to V-180;Q-167 to 1-181; A-168 to T-182; G-169 toK-183; R-170 to V-184; P-171 to T-185; N-172 to D-186; K-173 to S-187; P-174 to Y-188;D-175 to P-189; S-176 to E-190; 1-177 to P-191;T-178 to T-192; V-179 to Q-193; V-180 toL-194; 1-181 to L-195; T-182 to M-196; K-183 toG-197; V-184 to T-198; T-185 to K-199; D-186 to S-200; S-187 to V-201; Y-188 to C-202;P-189 to E-203; E-190 to V-204; P-191 to G-205;T-192 to S-206; Q-193 to N-207; L-194 toW-208; L-195 to F-209; M-196 to Q-210; G-197 to P-211; T-198 to 1-212; K-199 to Y-213; S-200 to L-214; V-201 to G-215; C-202 to A-216;E-203 to M-217; V-204 to F-218; G-205 toS-219; S-206 to L-220; N-207 to Q-221; W-208 to E-222; F-209 to G-223; Q-210 to D-224;P-211 to K-225; 1-212 to L-226; Y-213 toM-227; L-214 to V-228; G-215 to N-229; A-216 to V-230; M-217 to S-231; F-218 to D-232;S-219 to 1-233; L-220 to S-234; Q-221 to L-235;E-222 to V-236; G-223 to D-237; D-224 toY-238; K-225 to T-239; L-226 to K-240; M-227 to E-241; V-228 to D-242; N-229 to K-243;V-230 to T-244; S-231 to F-245; D-232 to F-246;I-233 to G-247; S-234 to A-248; L-235 to F-249;V-236 to L-250; D-237 to L-251; of SEQ ID NO:2 Polynucleotides encoding the above polypeptide fragments and antibodies that bind the above polypeptide fragments are also encompassed by the invention.

Detail Description Paragraph - DETX (124):

[0230] Moreover, the present invention further provides polypeptides having one or more residues deleted from the carboxy terminus of the amino acid sequence of the polypeptide shown in SEQ ID NO:4 (FIGS. 3A-3C). For example, the present invention provides polypeptides comprising, or alternatively consisting of, the amino acid sequence of residues 1-m.sup.1 of the amino acid sequence in SEQ ID NO:4, where ml is any integer in the range 6-416. More in particular, in certain embodiments, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group consisting of residues M-1 to G-416; M-1 to R-415; M-1 toQ-414; M-1 to L-413; M-1 to R-412; M-1 toS-411; M-1 to R-410; M-1 to L-409; M-1 toD-408; M-1 to E-407; M-1 to V-406; M-1 toC-405; M-1 to G-404; M-1 to D-403; M-1 toL-402; M-1 to G-401; M-1 to M-400; M-1 toR-399; M-1 to E-398; M-1 to L-397; M-1 toA-396; M-1 to A-395; M-1 to Y-394; M-1 toV-393; M-1 to A-392; M-1 to G-391; M-1 toL-390; M-1 to G-389; M-1 to A-388; M-1 toP-387; M-1 to Q-386; M-1 to Q-385; M-1 toQ-384; M-1 to R-383; M-1 to W-382; M-1 toR-381; M-1 to K-380; M-1 to L-379; M-1 toM-378; M-1 to E-377; M-1 to Y-376; M-1 toQ-375; M-1 to Q-374; M-1 to D-373; M-1 toR-372; M-1 to F-371; M-1 to R-370; M-1 toG-369; M-1 to 1-368; M-1 to E-367; M-1 toV-366; M-1 to E-365; M-1 to V-364; M-1 toA-363; M-1 to E-362; M-1 to 1-361; M-1 toE-360; M-1 to A-359; M-1 to E-358; M-1 toR-357; M-1 to L-356; M-1 to G-355; M-1 toL-354; M-1 to T-353; M-1 to R-352; M-1 toV-351; M-1 to F-350; M-1 to E-349; M-1 toK-348; M-1 to W-347; M-1 to R-346; M-1 toR-345; M-1 to A-344; M-1 to P-343; M-1 toV-342; M-1 to A-341; M-1 to D-340; M-1 toM-339; M-1 to V-338; M-1 to D-337; M-1 toY-336; M-1 to L-335; M-1 to Q-334; M-1 toP-333; M-1 to G-332; M-1 to P-331; M-1 toQ-330; M-1 to L-329; M-1 to M-328; M-1 toM-327; M-1 to A-326; M-1 to P-325; M-1 toS-324; M-1 to G-323; M-1 to A-322; M-1 toP-321; M-1 to S-320; M-1 to E-319; M-1 toP-318; M-1 to S-317; M-1 to L-316; M-1 toT-315; M-1 to P-314; M-1 to A-313; M-1 toA-312; M-l to A-311; M-1 to P-310; M-1 toG-309; M-1 to L-308; M-1 to A-307; M-1 toR-306; M-1 to S-305; M-1 to P-304; M-1 toL-303; M-1 to Q-302; M-1 to D-301; M-1 toW-300; M-1 to S-299; M-1 to W-298; M-1 toT-297; M-1 to V-296; M-1 to Q-295; M-1 toP-294; M-1 to C-293; M-1 to L-292; M-1 toA-291; M-1 to E-290; M-1 to Q-289; M-1 toT-288; M-1 to E-287; M-1 to P-286; M-1 toY-285; M-1 to G-284; M-1 to P-283; M-1 toT-282; M-1 to W-281; M-1 to S-280; M-1 toN-279; M-1 to G-278; M-1 to V-277; M-1 toL-276; M-1 to Q-275; M-1 to V-274; M-1 toT-273; M-1 to C-272; M-1 to 1-271; M-1 toK-270; M-1 to E-269; M-1 to S-268; M-1 toS-267; M-1 to D-266; M-1 to P-265; M-1 toP-264; M-1 to A-263; M-1 to L-262; M-1 toL-261; M-1 to T-260; M-1 to H-259; M-1 toA-258; M-1 to S-257; M-1 to D-256; M-1 toL-255; M-1 to P-254; M-1 to S-253; M-1 toL-252; M-1 to H-251; M-1 to T-250; M-1 toA-249; M-1 to P-248; M-1 to P-247; M-1 toP-246; M-1 to T-245; M-1 to L-244; M-1 toA-243; M-1 to E-242; M-1 to M-241; M-1 toG-240; M-1 to A-239; M-1 to E-238; M-1 toD-237; M-1 to A-236; M-1 to T-235; M-1 toV-234; M-1 to L-233; M-1 to P-232; M-1 toK-231; M-1 to H-230; M-1 to P-229; M-1 toW-228; M-1 to C-227; M-1 to H-226; M-1 toR-225; M-1 to Y-224; M-1 to T-223; M-1 toY-222; M-1 to T-221; M-1 to L-220; M-1 toT-219; M-1 to A-218; M-1 to G-217; M-1 toL-216; M-1 to L-215; M-1 to L-214; M-1 toP-213; M-1 to V-212; M-1 to V-211; M-1 toL-210; M-1 to G-209; M-1 to A-208; M-1 toL-207; M-1 to L-206; M-1 to V-205; M-1 toQ-204; M-1 to V-203; M-1 to W-202; M-1 toF-201; M-1 to M-200; M-1 to Q-199; M-1 toR-198; M-1 to W-197; M-1 to G-196; M-1 toC-195; M-1 to V-194; M-1 to A-193; M-1 toA-192; M-1 to C-191; M-1 to R-190; M-1 toE-189; M-1 to P-188; M-1 to C-187; M-1 toS-186; M-1 to G-185; M-1 to L-184; M-1 toT-183; M-1 to S-182; M-1 to T-181; M-1 toP-180; M-1 to C-179; M-1 to S-178; M-1 toV-177; M-1 to C-176; M-1 to G-175; M-1 toD-174; M-1 to G-173; M-1 to H-172; M-1 toE-171; M-1 to Y-170; M-1 to F-169; M-1 toG-168; M-1 to P-167; M-1 to L-166; M-1 toC-165; M-1 to T-164; M-1 to G-163; M-1 toC-162; M-1 to D-161; M-1 to T-160; M-1 toD-159; M-1 to R-158; M-1 to R-157; M-1 toS-156; M-1 to C-155; M-1 to L-154; M-1 toL-153; M-1 to R-152; M-1 to T-151;

M-1 toH-150; M-1 to R-149; M-1 to H-148; M-1 toL-147; M-1 to A-146; M-1 to G-145; M-1 toC-144; M-1 to D-143; M-1 to L-142; M-1 toC-141; M-1 to P-140; M-1 to Q-139; M-1 toC-138; M-1 to Y-137; M-1 to F-136; M-1 toP-135; M-1 to S-134; M-1 to S-133; M-1 toS-132; M-1 to V-131; M-1 to C-130; M-1 toQ-129; M-1 to S-128; M-1 to V-127; M-1 toQ-126; M-1 to C-125; M-1 to E-124; M-1 toV-123; M-1 to F-122; M-1 to W-121; M-1 toG-120; M-1 to P-119; M-1 to K-118; M-1 toC-117; M-1 to G-116; M-1 to C-115; M-1 toR-114; M-1 to T-113; M-1 to D-112; M-1 toA-111; M-1 to V-110; M-1 to A-109; M-1 toS-108; M-1 to C-107; M-1 to N-106; M-1 toE-105; M-1 to L-104; M-1 to A-103; M-1 toV-102; M-1 to Q-101; M-1 to S-100; M-1 toA-99; M-1 to Q-98; M-1 to E-97; M-1 to D-96;M-1 to C-95; M-1 to A-94; M-I to Q-93; M-1 toC-92; M-1 to R-91; M-1 to A-90; M-I to C-89;M-1 to E-88; M-1 to S-87; M-1 to N-86; M-1 toH-85; M-1 to H-84; M-1 to N-83; M-1 to E-82;M-1 to W-81; M-1 to A-80; M-1 to L-79; M-1 toF-78; M-1 to T-77; M-1 to D-76; M-1 to Q-75;M-1 to P-74; M-I to C-73; M-I to V-72; M-1 toL-71; M-1 to C-70; M-1 to T-69; M-1 to S-68;M-1 to N-67; M-1 to G-66; M-1 to C-65; M-1 toP-64; M-1 to E-63; M-1 to T-62; M-1 to C-61;M-1 to P-60; M-1 to A-59; M-1 to K-58; M-1 toL-57; M-1 to Y-56; M-1 to H-55; M-1 to G-54;M-1 to A-53; M-1 to P-52; M-1 to C-51; M-1 toG-50; M-1 to R-49; M-1 to C-48; M-1 to C-47;M-1 to F-46; M-1 to L-45; M-1 to G-44; M-1 toI-43; M-1 to K-42; M-1 to K-41; M-1 to H-40;M-1 to F-39; M-1 to D-38; M-1 to G-37; M-1 toA-36; M-1 to C-35; M-1 to D-34; M-1 to C-33;M-1 to R-32; M-1 to P-31; M-1 to S-30; M-1 toR-29; M-1 to T-28; M-1 to G-27; M-1 to G-26;M-1 to Q-25; M-1 to A-24; M-1 to R-23; M-1 toA-22; M-1 to G-21; M-1 to L-20; M-1 to L-19;M-1 to V-18; M-1 to L-17; M-1 to L-16; M-1 toL-15; M-1 to A-14; M-1 to A-13; M-1 to A-12;M-1 to V-11; M-1 to A-10; M-1 to A-9; M-1 toC-8; M-1 to G-7; M-1 to R-6; of SEQ ID NO:4. Polynucleotides encoding the above polypeptide fragments and antibodies that bind the above polypeptide fragments are also encompassed by the invention.

Detail Description Paragraph - DETX (126):

[0232] The invention also provides polypeptides having one or more amino acids deleted from both the amino and the carboxyl termini of the polypeptide of SEQ ID NO:4 (FIGS. 3A-3C). For example, amino terminal and carboxyl terminal deletions of the polypeptide sequence may be described generally, for example, as having residues n.sup.1-m.sup.1 of SEQ ID NO:2 where n.sup.1 is an integer in the range of 1-403 and m.sup.1 is an integer in the range of 15-417. For example, and more in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group consisting of residues of M-1 to L-15; E-2 to L-16; Q-3 to L-17; R-4 toV-18; P-5 to L-19; R-6 to L-20; G-7 to G-21; C-8 to A-22; A-9 to R-23; A-10 to A-24; V-11 toQ-25; A-12 to G-26; A-13 to G-27; A-14 to T-28;L-15 to R-29; L-16 to S-30; L-17 to P-31; V-18 to R-32; L-19 to C-33; L-20 to D-34; G-21 toC-35; A-22 to A-36; R-23 to G-37; A-24 to D-38;Q-25 to F-39; G-26 to H-40; G-27 to K-41; T-28 to K-42; R-29 to 1-43; S-30 to G-44; P-31 toL-45; R-32 to F-46; C-33 to C-47; D-34 to C-48;C-35 to R-49; A-36 to G-50; G-37 to C-51; D-38 to P-52; F-39 to A-53; H-40 to G-54; K-41 toH-55; K-42 to Y-56; 1-43 to L-57; G-44 to K-58;L-45 to A-59; F-46 to P-60; C-47 to C-61; C-48 to T-62; R-49 to E-63; G-50 to P-64; C-51 toC-65; P-52 to G-66; A-53 to N-67; G-54 to S-68;H-55 to T-69; Y-56 to C-70; L-57 to L-71; K-58 to V-72; A-59 to C-73; P-60 to P-74; C-61 toQ-75; T-62 to D-76; E-63 to T-77; P-64 to F-78;C-65 to L-79; G-66 to A-80; N-67 to W-81; S-68 to E-82; T-69 to N-83; C-70 to H-84; L-71 toH-85; V-72 to N-86; C-73 to S-87; P-74 to E-88;Q-75 to C-89; D-76 to A-90; T-77 to R-91; F-78 to C-92; L-79 to Q-93; A-80 to A-94; W-81 toC-95; E-82 to D-96; N-83 to E-97; H-84 to Q-98;H-85 to A-99; N-86 to S-100; S-87 to Q-101; E-88 to V-102; C-89 to A-103; A-90 to L-104;R-91 to E-105; C-92 to N-106; Q-93 to C-107;A-94 to S-108; C-95 to A-109; D-96 to V-110; E-97 to A-111; Q-98 to D-112; A-99 to T-113;S-100 to R-114; Q-101 to C-115; V-102 toG-116; A-103 to C-117; L-104 to K-118; E-105 to P-119; N-106 to G-120; C-107 to W-121;S-108 to F-122; A-109 to V-123; V-110 toE-124; A-111 to C-125; D-112

to Q-126; T-113 to V-127; R-114 to S-128; C-115 to Q-129;G-116 to C-130; C-117 to V-131; K-118 toS-132; P-119 to S-133; G-120 to S-134; W-121 to P-135; F-122 to F-136; V-123 to Y-137; E-124 to C-138; C-125 to Q-139; Q-126 to P-140;V-127 to C-141; S-128 to L-142; Q-129 toD-143; C-130 to C-144; V-131 to G-145; S-132 to A-146; S-133 to L-147; S-134 to H-148; P-135 to R-149; F-136 to H-150; Y-137 to T-151;C-138 to R-152; Q-139 to L-153; P-140 toL-154; C-141 to C-155; L-142 to S-156; D-143 to R-157; C-144 to R-158; G-145 to D-159;A-146 to T-160; L-147 to D-161; H-148 toC-162; R-149 to G-163; H-150 to T-164; T-151 to C-165; R-152 to L-166; L-153 to P-167; L-154 to G-168; C-155 to F-169; S-156 to Y-170;R-157 to E-171; R-158 to H-172; D-159 toG-173; T-160 to D-174; D-161 to G-175; C-162 to C-176; G-163 to V-177; T-164 to S-178;C-165 to C-179; L-166 to P-180; P-167 to T-181;G-168 to S-182; F-169 to T-183; Y-170 to L-184;E-171 to G-185; H-172 to S-186; G-173 toC-187; D-174 to P-188; G-175 to E-189; C-176 to R-190; V-177 to C-191; S-178 to A-192;C-179 to A-193; P-180 to V-194; T-181 toC-195; S-182 to G-196; T-183 to W-197; L-184 to R-198; G-185 to Q-199; S-186 to M-200;C-187 to F-201; P-188 to W-202; E-189 toV-203; R-190 to Q-204; C-191 to V-205; A-192 to L-206; A-193 to L-207; V-194 to A-208;C-195 to G-209; G-196 to L-210; W-197 toV-211; R-198 to V-212; Q-199 to P-213; M-200 to L-214; F-201 to L-215; W-202 to L-216;V-203 to G-217; Q-204 to A-218; V-205 toT-219; L-206 to L-220; L-207 to T-221; A-208 toY-222; G-209 to T-223; L-210 to Y-224; V-21Ito R-225; V-212 to H-226; P-213 to C-227;L-214 to W-228; L-215 to P-229; L-216 toH-230; G-217 to K-231; A-218 to P-232; T-219 to L-233; L-220 to V-234; T-221 to T-235; Y-222 to A-236; T-223 to D-237; Y-224 to E-238;R-225 to A-239; H-226 to G-240; C-227 toM-241; W-228 to E-242; P-229 to A-243; H-230 to L-244; K-231 to T-245; P-232 to P-246; L-233 to P-247; V-234 to P-248; T-235 to A-249;A-236 to T-250; D-237 to H-251; E-238 toL-252; A-239 to S-253; G-240 to P-254; M-241 to L-255; E-242 to D-256; A-243 to S-257; L-244 to A-258; T-245 to H-259; P-246 to T-260; P-247 to L-261; P-248 to L-262; A-249 to A-263; T-250 to P-264; H-251 to P-265; L-252 to D-266; S-253 to S-267; P-254 to S-268; L-255 to E-269; D-256 to K-270; S-257 to I-271; A-258 to C-272;H-259 to T-273; T-260 to V-274; L-261 toQ-275; L-262 to L-276; A-263 to V-277; P-264 to G-278; P-265 to N-279; D-266 to S-280;S-267 to W-281; S-268 to T-282; E-269 toP-283; K-270 to G-284; 1-271 to Y-285; C-272 to P-286; T-273 to E-287; V-274 to T-288;Q-275 to Q-289; L-276 to E-290; V-277 toA-291; G-278 to L-292; N-279 to C-293; S-280 to P-294; W-281 to Q-295; T-282 to V-296;P-283 to T-297; G-284 to W-298; Y-285 toS-299; P-286 to W-300; E-287 to D-301; T-288 to Q-302; Q-289 to L-303; E-290 to P-304;A-291 to S-305; L-292 to R-306; C-293 toA-307; P-294 to L-308; Q-295 to G-309; V-296 to P-310; T-297 to A-311; W-298 to A-312;S-299 to A-313; W-300 to P-314; D-301 toT-315; Q-302 to L-316; L-303 to S-317; P-304 toP-318; S-305 to E-319; R-306 to S-320; A-307 toP-321; L-308 to A-322; G-309 to G-323; P-310 to S-324; A-311 to P-325; A-312 to A-326;A-313 to M-327; P-314 to M-328; T-315 toL-329; L-316 to Q-330; S-317 to P-331; P-318 toG-332; E-319 to P-333; S-320 to Q-334; P-321 to L-335; A-322 to Y-336; G-323 to D-337;S-324 to V-338; P-325 to M-339; A-326 toD-340; M-327 to A-341; M-328 to V-342; L-329 to P-343; Q-330 to A-344; P-331 to R-345;G-332 to R-346; P-333 to W-347; Q-334 toK-348; L-335 to E-349; Y-336 to F-350; D-337 to V-351; V-338 to R-352; M-339 to T-353;D-340 to L-354; A-341 to G-355; V-342 toL-356; P-343 to R-357; A-344 to E-358; R-345 toA-359; R-346 to E-360; W-347 to 1-361; K-348 to E-362; E-349 to A-363; F-350 to V-364;V-351 to E-365; R-352 to V-366; T-353 toE-367; L-354 to 1-368; G-355 to G-369; L-356 toR-370; R-357 to F-371; E-358 to R-372; A-359 to D-373; E-360 to Q-374; 1-361 to Q-375; E-362 to Y-376; A-363 to E-377; V-364 to M-378;E-365 to L-379; V-366 to K-380; E-367 toR-381; 1-368 to W-382; G-369 to R-383; R-370 to Q-384; F-371 to Q-385; R-372 to Q-386;D-373 to P-387; Q-374 to A-388; Q-375 toG-389; Y-376 to L-390; E-377 to G-391; M-378 to A-392; L-379 to V-393; K-380 to Y-394;R-381 to A-395; W-382 to A-396; R-383 toL-397; Q-384 to E-398; Q-385 to R-399; Q-386 to M-400; P-387 to G-401; A-388 to L-402;G-389 to D-403; L-390 to G-404; G-391 toC-405; A-392 to V-406; V-393 to E-407; Y-394 to D-408; A-395 to L-409; A-396 to R-410;L-397 to S-411; E-398 to R-412; R-399 to L-413;M-400 to Q-414; G-401 to R-415; L-402 toG-416; or D-403 to P-417 of SEQ ID NO:4. Polynucleotides encoding the above

polypeptide fragments and antibodies that bind the above polypeptide fragments are also encompassed by the invention.

Detail Description Paragraph - DETX (273):

[0379] The present invention further encompasses antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent. The antibodies can be used diagnostically to, for example, monitor the development or progression of a tumor as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. Detectioncan be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions. The detectable substance may be coupled or conjugated either directly to the antibody (or fragment thereof) or indirectly, through an intermediate (such as, for example, a linker known in the art) using techniques known in the art. See, for example, U.S. Pat. No. 4,741,900 for metal ions which can be conjugated to antibodies for use as diagnostics according to the present invention. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include .sup.125I, .sup.131I, .sup.111In or .sup.99Tc.

Detail Description Paragraph - DETX (284):

[0390] The antibodies of the invention may be assayed for immunospecific binding by any method known in the art. The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few. Such assays are routine and well known in the art (see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, which is incorporated by reference herein in its entirety). Exemplary immunoassays are described briefly below (but are not intended by way of limitation).

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ABSTRACT:

The arming of activated T cells (ATC) with BiAbs can overcome major barriers for successful adoptive immunotherapy. The BiAb approach takes the advantage of the targeting specificity of monoclonal antibodies and the cytotoxic capacity of T cells to lyse tumors. Arming of ATC with BiAb makes every T cell an antigen-specific CTL and infusions of such cells will markedly increase the effective precursor frequency of CTL in the cancer patient. Furthermore, the ability of such armed ATC to kill multiple times without rearming with BiAb, secrete tumoricidal cytokines, secrete chemokines, and survive in patients for up to 8 days after the last infusion or in Beige/SCID mice for over 13 weeks after cessation of treatment. The persistence of cells in the Beige/SCID after infusion show long-term survival capability in the host. Re-stimulation of armed ATC after 3 cycles of cytotoxicity with tumor cells resulted in the secretion of interferon gamma indicating the development of tumor specific immune responses in the population of cells that have been exposed multiple times to antigen. In summary, armed ATC can act as a cytotoxic "drug", kill multiple times (direct killing), divide after killing (increasing the effector:target ratio in vivo), secrete tumoricidal cytokines (indirectly killing), secrete chemokines at the tumor site (recruit nave T cells and antigen-presenting cells to immunize the patient to tumor lysate) and persist in patients and animal models for weeks to months (long-term survival).

[0001] This application claims priority to U.S. Provisional Application Serial No. 60/313,164 filed Aug. 17, 2001, the entirety of which is incorporated by reference herein.

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Detail Description Paragraph - DETX (10):

[0077] In a preferred embodiment, the ATC or COACTs undergo multiple cycles of tumor antigen recognition and tumor cell killing. The ability of these ATC or COACTs to kill multiple cells is shown in the examples which follow. Assays used to identify the ATC and/or COACTs and determine their ability to kill tumor cells is discussed in great detail infra and in the examples which follow. For example, an armed T cell which is targeted to tumor antigens such as, for example, Her2.sup.+ tumors, can be identified by labeling the T cell with a fluorescent marker, or secondary antibody that is detectable by flow cytometry or other methods well-known to one of ordinary skill in the art. Examples of labels for detection of the armed T cells include but not limited to, green fluorescent proteins, avidins and the like. As an illustrative example, biopsies from a tumor to which tumor specific T cells armed with bispecific antibodies and labeled with a detectable marker, are used to confirm the presence of the armed T cells at the site of the tumor. The biopsied tissue is processed by methods well known in the art and prepared for use in cell detection assays.

Detail Description Paragraph - DETX (127):

[0193] The term "fluorescent component" or "fluorescent label" or "labeled" refers to a component capable of absorbing light and then re-emitting at least some fraction of that energy as light over time. The term includes discrete compounds, molecules, naturally fluorescent proteins and macro-molecular complexes or mixtures of fluorescent and non-fluorescent compounds or molecules. The term "fluorescent component" or "fluorescent label" also includes components that exhibit long lived fluorescence decay such as lanthanide ions and lanthanide complexes with organic ligand sensitizes, that absorb light and then re-emit the energy over milliseconds. Other labels include different fluorochromes and fluorescent proteins such as green fluorescent protein. Fluorochromes which may find use in a multicolor analysis include phycobiliproteins, e.g., phycoerythrin and allophycocyanins; fluorescein and Texas red.

Detail Description Paragraph - DETX (443):

[0469] 23. Rosenberg, S. A., B. S. Packard, P. M. Aebersold, D. Solomon, S. L. Topalian, S. T. Toy, P. Simon, M. T. Lotze, J. C. Yang, C. A. Seipp, C. G. Simpson, C. Carter, S. Bock, D. Schwartzentruber, J. P. Wei, and D. E. White. 1988. N. Engl. J. Med. 319:1676-1680.

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DOCUMENT-IDENTIFIER: US 20030175705 A1

TITLE: Methods of use for novel single nucleotide polymorphisms of olfactory receptor-like polypeptides and nucleic acids encoding the same

PUBLICATION-DATE: September 18, 2003

INVENTOR-INFORMATION:

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DATE FILED: October 9, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60323755 20010920 US

US-CL-CURRENT: 435/6, 435/7.2

ABSTRACT:

The present invention provides novel methods of use for nucleic acid sequences having single nucleotide polymorphisms that encode olfactory receptor-like polypeptides and the polypeptides so encoded. Also provided are methods of use for any derivative, variant, mutant or fragment forms of these polypeptides or polynucleotides.

RELATED APPLICATIONS

[0001] This application claims the benefit of priority to Provisional Application U.S. Serial No. 60/ _____, filed Sep. 20, 2001, hereby incorporated by reference in its entirety.

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Summary of Invention Paragraph - BSTX (31):

[0028] Issel-Tarver and Rine characterized 4 members of the canine olfactory receptor gene family (Issel-Tarver and Rine, "Organization and expression of canine olfactory genes." 93(20) PNAS, USA 10897-902 (Oct. 1, 1996)). The 4 subfamilies comprised genes expressed exclusively in olfactory epithelium. Analysis of large DNA fragments using Southern blots of pulsed field gels indicated that subfamily members were clustered together, and that two of the subfamilies were closely linked in the dog genome. Analysis of the four

olfactory receptor gene subfamilies in 26 breeds of dog provided evidence that the number of genes per subfamily was stable in spite of differential selection on the basis of olfactory acuity in scent hounds, sight hounds, and toy breeds.

Summary of Invention Paragraph - BSTX (296):

[0293] Following Klenow polymerase-mediated base incorporation, PPi is released and used as a substrate, together with adenosine 5'-phosphosulfate (APS), for ATP sulfurylase, which results in the formation of ATP. Subsequently, the ATP accomplishes the conversion of luciferin to its oxi-derivative by the action of luciferase. The ensuing light output becomes proportional to the number of added bases, up to about four bases. To allow processivity of the method dNTP excess is degraded by apyrase, which is also present in the starting reaction mixture, so that only dNTPs are added to the template during the sequencing. The process has been fully automated and adapted to a 96-well format, which allows rapid screening of large SNP panels.

Summary of Invention Paragraph - BSTX (413):

[0410] In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to a NOVX protein determined. The cell, for example, can be of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the NOVX protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the NOVX protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with .sup.125I, .sup.35S, .sup.14C, or .sup.3H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds NOVX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a NOVX protein, wherein determining the abilitv of the test compound to interact with a NOVX protein comprises determining the ability of the test compound to preferentially bind to NOVX protein or a biologically-active portion thereof as compared to the known compound.

Summary of Invention Paragraph - BSTX (415):

[0412] Determining the ability of the NOVX protein to bind to or interact with a NOVX target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the ability of the NOVX protein to bind to or interact with a NOVX target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (i e. intracellular Ca.sup.2+, diacylglycerol, IP.sub.3, etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the induction of a reporter gene (comprising a NOVX-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, e g, luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

Summary of Invention Paragraph - BSTX (441):

[0438] An antibody specific for a protein of the invention can be used to isolate the protein by standard techniques, such as immunoaffinity chromatography or immunoprecipitation. Such an antibody can facilitate the purification of the natural protein antigen from cells and of recombinantly produced antigen expressed in host cells. Moreover, such an antibody can be used to detect the antigenic protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the antigenic protein. Antibodies directed against the protein can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase alkaline phosphatase, .beta.-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include .sup.125I, .sup.131I, .sup.35S or .sup.3H.

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PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030154502 A1

TITLE: Universal markers of transgenesis

PUBLICATION-DATE: August 14, 2003

INVENTOR-INFORMATION:

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APPL-NO: 10/ 360222

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RELATED-US-APPL-DATA:

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parent-patent 6518481 US

US-CL-CURRENT: 800/8, 800/14 , 800/19 , 800/20 , 800/21

ABSTRACT:

The invention relates to methods, cells and nucleic acids for making transgenic animals. The methods generally comprise introducing into a genome of an animal a genetic construct comprising a transcriptional regulatory element operably linked to a heterologous marker gene encoding a marker, wherein the element drives expression of the marker across genera transgenic in the construct sufficient to visually detect the marker in photoreceptive cells or organs, and selecting for transgenesis by visually detecting the marker in a photoreceptive cell or organ of the animal.

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application claims priority under 35USC120 to U.S. Ser. No. 09/373,129, having the same title and inventors, filed on Aug. 12, 1999, now U.S. Pat. No. 6,518,481, which is incorporated herein by reference.

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Summary of Invention Paragraph - BSTX (8):

[0007] The subject methods generally comprise (a) introducing into a genome of an animal a genetic construct comprising a transcriptional regulatory element operably linked to a heterologous marker gene encoding a marker, wherein the element drives expression of the marker across genera transgenic in the construct sufficient to visually detect the marker in photoreceptive cells or organs, and (b) selecting for transgenesis by visually detecting the marker in a photoreceptive cell or organ of the animal. In particular embodiments,

the construct comprises a vector, such as transposon or retrovirus, particularly a polytropic vector. The construct may integrate into the genome by homologous or non-homologous recombination. In particular embodiments, the transcriptional regulatory element comprises a binding site selected from a Pax-6 binding site, a Glass binding site, etc., particularly a plurality of P3 sites, and the marker is a fluorescent protein, particularly a green fluorescent protein or variant thereof.

Summary of Invention Paragraph - BSTX (13):

[0011] To drive marker expression in a series of diverged organisms requires a promoter which is active in a wide range of species. Furthermore, to avoid problems with low expression and the interference of autofluorescence, a regional specific promoter is preferable over a constitutively active one. A wide variety of regulatory elements may be employed, so long as they meet the requisite functional limitations. These may be natural promoter elements, naturally driving gene expression in photoreceptive cells or organs, elements derived from such natural promoter elements by mutational selection or consensus sequences, synthetic elements derived by iterative selection process, e.g. SELEX procedures, etc. In a particular embodiment, the element comprises a binding site selected from a Pax-6, a Pax-6 like binding site such as a twin-of-eyeless (TOY) binding site, a Glass binding site, etc. In more particular embodiments, the element comprises a Pax-6 Paired Domain or Homeodomain binding site, more particularly a P3 site, wherein the P3 site comprises the sequence: TAATYNRATTA (SEQ ID NO:01), wherein Y=C or T; R=G or A; N=any nucleotide (Wilson et al., 1993, Genes Dev 7, 2120-34; Czemy and Busslinger, 1995, Mol Cell Biol 15, 2858-71). Tables 1-6 provide other exemplary transcriptional regulatory element binding sites functional in the subject methods. Pax-6 binding sites are of particular interest due to the evolutionary conserved role Pax-6-homologs play in eye development across different phyla (Callaerts et al., 1997, Annu Rev Neurosci 20, 483-532).

Summary of Invention Paragraph - BSTX (22):

[0020] The construct includes a marker gene encoding a marker which, when expressed in the transgenic animal, is visually detectable in a photoreceptive cell or organ of the animal. Criteria for marker selection include detectability, physiological and method compatibility, e.g. smaller sized marker genes enable small transposon constructs resulting in high transformation rates. A wide variety of markers may be encoded, including ribozymes or protein enzymes such as galactosidase, luciferase (e.g. Wilson and Hastings, 1998, Annu Rev Cell Dev Biol 14, 197-230), etc., and particularly directly detectable proteins, more particularly fluorescent proteins, especially commercially available enhanced fluorescent proteins (e.g. EGFP, ECFP and EYFP, Clontech Laboratories, Inc.).

Summary of Invention Paragraph - BSTX (23):

[0021] Fluorescent proteins may comprise naturally occurring, engineered (i.e., analogs) and/or synthetic sequences. For example, many cnidarians use natural green fluorescent proteins ("GFPs") as energy-transfer acceptors in bioluminescence. Natural GFPs have been isolated from numerous animals, including the Pacific Northwest jellyfish, Aequorea victoria, the sea pansy, Renilla reniformis, and Phialidium gregarium; Ward et al., Photochem. Photobiol., 35:803-808 (1982); Levine et al., Comp. Biochem. Physiol., 72B:77-85 (1982). In addition, a variety of Aequorea-related fluorescent proteins having useful excitation and emission spectra have been engineered by modifying the amino acid sequence of a naturally occurring GFP from Aequorea victoria (Prasher et al., Gene, 111:229-233 (1992); Heim et al., Proc. Natl. Acad. Sci., USA, 91:12501-04 (1994). Particularly useful are GFPs from or

which derive from the jellyfish A. victoria (see e.g. U.S. Pat. No. 5,491,084 for applicable such GFPs) and include variants offering a variety of different excitation and emission wavelengths; see e.g. Heim and Tsein, 1996, Current Biology 6, 178-182. Exemplary amino acid variants include F64L, S65T, Y66W, N1461, M153T, V163A and N212K, and combinations thereof. For example, CFP is the GFP of Aequorea victoria with the following additional mutations: F64L, S65T, Y66W, N1461, M153T, V163A, N212K (Miyawaki et al., 1997, Nature 388:882-7), and YFP is the GFP of A. Victoria with the following additional mutations: S65G, V68L, S72A, T203Y (Cubitt et al., 1999, Methods Cell Biol 58, 19-30). Accordingly, in preferred embodiments, the marker is a Aequorea or Aequorea-related fluorescent protein, see U.S. Pat. No. 5,912,137 for applicable sequence, scope, definitions and examples.

Summary of Invention Paragraph - BSTX (24):

[0022] Suitable fluorescent proteins may also derive from other sources, and include the yellow fluorescent protein from Vibrio fischeri strain Y-1 (Baldwin et al., Biochemistry (1990) 29:5509-15) which requires flavins as fluorescent co-factors; Peridinin-chlorophyll, a red fluorescing binding protein from the dinoflagellate Symbiodinium sp. (Morris et al., Plant Mol Biol, (1994) 24:673:77); phycobiliproteins from marine cyanobacteria such as Synechococcus, e.g., phycoerythrin and phycocyanin (Wilbanks et al., J. Biol. Chem. (1993) 268:1226-35), yellow to red fluorescing proteins which require phycobilins as fluorescent co-factors.

Summary of Invention - Table CWU - BSTL (7):

7TABLE 7 Exemplary transgenic expression-marker detection systems Vector Element Marker Host Epression hobo 3xP3-hsp70 TATA EGFP drosophila ++++ Hermes 9xP2-hsp70 TATA ECFP tribolium ++++ piggyBac 3x(P2 + PD)-hsp70 TATA EYFP grasshopper ++++ Himar1 6x(P2 + PD-hsp70 TATA luciferase zebrafish ++++ piggyBac 3xP3-hsp70 TATA EGFP chicken ++++ MLV > VSVG 3xP3-hsp70 TATA EGFP mouse ++++ AcNPV 3xP3-hsp70 TATA EGFP human ++++ piggyBac 3xP3-hsp70 TATA EGFP cockroach ++++ mariner 3xP3-hsp70 TATA EGFP honeybee ++++ Hermes 3xP3-hsp70 TATA EGFP mosquito ++++ piggyBac 3xP3-hsp70 TATA EGFP shrimp ++++ Himar1 3xP3-Adeno MLP TATA EGFP lobster ++++ piggyBac 3xP3-Adeno MLP TATA EGFP termite ++++ AcNPV > VSVG 3xP3-Adeno MLP TATA EGFP bollworm ++++ piggyBac 3xP3-Adeno MLP TATA EGFP fire ant ++++ minos 3xP3-Adeno MLP TATA EGFP med. fly ++++

Claims Text - CLTX (14):

13. A method according to claim 1, wherein the element comprises a plurality of Pax-6 binding sites and said Pax-6 binding sites comprise twin-of-eyeless (TOY) binding sites.

Claims Text - CLTX (16):

15. A method according to claim 1, wherein the marker is a fluorescent protein.

Claims Text - CLTX (17):

16. A method according to claim 1, wherein the marker is a fluorescent protein and said fluorescent protein is a green fluorescent protein.

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DOCUMENT-IDENTIFIER: US 20030091563 A1

TITLE: Novel GPCR-proteins and nucleic acids encoding same

PUBLICATION-DATE: May 15, 2003

INVENTOR-INFORMATION:

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DATE FILED: April 11, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60195994 20000411 US

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non-provisional-of-provisional 60220644 20000725 US

non-provisional-of-provisional 60264851 20010129 US

non-provisional-of-provisional 60199964 20000427 US

non-provisional-of-provisional 60268567 20010214 US

non-provisional-of-provisional 60199955 20000427 US

non-provisional-of-provisional 60259641 20010104 US

non-provisional-of-provisional 60200176 20000427 US

non-provisional-of-provisional 60199948 20000427 US

non-provisional-of-provisional 60199956 20000427 US

non-provisional-of-provisional 60218995 20000717 US

US-CL-CURRENT: 424/143.1, 435/320.1 , 435/325 , 435/69.1 , 530/350 , 530/388.22 , 536/23.5

ABSTRACT:

Disclosed herein are nucleic acid sequences that encode G-coupled protein-receptor related polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivatives, variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Ser. No. 60/195,994, filed Apr. 11, 2000 (15966-767); U.S. Ser. No. 60/196,538, filed Apr. 11, 2000 (15966-768); U.S. Ser. No. 60/220,644, filed Jul. 25, 2000 (15966-768A); U.S. Ser. No. 60/264,851, filed Jan. 29, 2001 (15966-768B); U.S. Ser. No. 60/199,964, filed Apr. 27, 2000 (15966-784); U.S. Ser. No. 60/268,567, filed Feb. 14, 2001 (15966-784A); U.S. Ser. No. 60/199,955, filed Apr. 27, 2000 (15966-785); U.S. Ser. No 60/259,641, filed Jan. 4, 2001 (15966-785A); U.S. Ser. No. 60/200,176, filed Apr. 27, 2000 (15966-786); U.S. Ser. No. 60/199,948, filed Apr. 27, 2000 (15966-787); U.S. Ser. No. 60/199,956, filed Apr. 27, 2000 (15966-788), and U.S. Ser. No. 60/218,995, filed Jul. 17, 2000 (15966-788A), which are incorporated herein by reference in their entirety.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (29):

[0026] Issel-Tarver and Rine (1996) characterized 4 members of the canine olfactory receptor gene family. The 4 subfamilies comprised genes expressed exclusively in olfactory epithelium. Analysis of large DNA fragments using Southern blots of pulsed field gels indicated that subfamily members were clustered together, and that two of the subfamilies were closely linked in the dog genome. Analysis of the four olfactory receptor gene subfamilies in 26 breeds of dog provided evidence that the number of genes per subfamily was stable in spite of differential selection on the basis of olfactory acuity in scent hounds, sight hounds, and toy breeds. Issel-Tarver and Rine (1997) performed a comparative study of four subfamilies of olfactory receptor genes first identified in the dog to assess changes in the gene family during mammalian evolution, and to begin linking the dog genetic map to that of humans. These four families were designated by them OLF1, OLF2, OLF3, and OLF4 in the canine genome. The subfamilies represented by these four genes range in size from 2 to 20 genes. They are all expressed in canine olfactory epithelium but were not detectably expressed in canine lung, liver, ovary, spleen, testis, or tongue. The OLF1 and OLF2 subfamilies are tightly linked in the dog genome and also in the human genome. The smallest family is represented by the canine OLF1 gene. Using dog gene probes individually to hybridize to Southern blots of genomic DNA from 24 somatic cell hybrid lines. They showed that the human homologous OLF1 subfamily maps to human chromosome 11. The human gene with the strongest similarity to the canine OLF2 gene also mapped to chromosome 11. Both members of the human subfamily that hybridized to canine OLF3 were located on chromosome 7. It was difficult to determine to which chromosome or chromosomes the human genes that hybridized to the canine OLF4 probe mapped. This subfamily is large in mouse and hamster as well as human, so the rodent background largely obscured the human cross-hybridizing bands. It was possible, however, to discern some human-specific bands in blots corresponding

to human chromosome 19. They refined the mapping of the human OLF1 homolog by hybridization to YACs that map to 11q11. In dogs, the OLF1 and OLF2 subfamilies are within 45 kb of one another (Issel-Tarver and Rine (1996)).

Summary of Invention Paragraph - BSTX (284):

[0281] In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to a NOVX protein determined. The cell, for example, can be of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the NOVX protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the NOVX protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with .sup.125I, .sup.35S, .sup.14C, or .sup.3H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds NOVX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a NOVX protein, wherein determining the ability of the test compound to interact with a NOVX protein comprises determining the ability of the test compound to preferentially bind to NOVX protein or a biologically-active portion thereof as compared to the known compound.

Summary of Invention Paragraph - BSTX (286):

[0283] Determining the ability of the NOVX protein to bind to or interact with a NOVX target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the ability of the NOVX protein to bind to or interact with a NOVX target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (i.e. intracellular Ca.sup.2+, diacylglycerol, IP.sub.3, etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the induction of a reporter gene (comprising a NOVX-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, e.g., luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

Summary of Invention Paragraph - BSTX (313):

[0310] An antibody specific for a protein of the invention can be used to isolate the protein by standard techniques, such as immunoaffinity chromatography or immunoprecipitation. Such an antibody can facilitate the purification of the natural protein antigen from cells and of recombinantly produced antigen expressed in host cells. Moreover, such an antibody can be used to detect the antigenic protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the antigenic protein. Antibodies directed against the protein can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given

treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, .beta.-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include .sup.125I, .sup.131I, .sup.35S or .sup.3H.

Detail Description Paragraph - DETX (20):

[0375] In brief, Pyrosequencing is a real time primer extension process of genotyping. This protocol takes double-stranded, biotinylated PCR products from genomic DNA samples and binds them to streptavidin beads. These beads are then denatured producing single stranded bound DNA. SNPs are characterized utilizing a technique based on an indirect bioluminometric assay of pyrophosphate (PP.sub.i) that is released from each dNTP upon DNA chain elongation. Following Klenow polymerase-mediated base incorporation, PP.sub.i is released and used as a substrate, together with adenosine 5'-phosphosulfate (APS), for ATP sulfurylase, which results in the formation of ATP. Subsequently, the ATP accomplishes the conversion of luciferin to its oxi-derivative by the action of luciferase. The ensuing light output becomes proportional to the number of added bases, up to about four bases. To allow processivity of the method dNTP excess is degraded by apyrase, which is also present in the starting reaction mixture, so that only dNTPs are added to the template during the sequencing. The process has been fully automated and adapted to a 96-well format, which allows rapid screening of large SNP panels.

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TITLE: Novel polypeptides and nucleic acids encoding same

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INVENTOR-INFORMATION:

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non-provisional-of-provisional 60180511 20000207 US

non-provisional-of-provisional 60180630 20000207 US

non-provisional-of-provisional 60220594 20000725 US

non-provisional-of-provisional 60181013 20000208 US

non-provisional-of-provisional 60181043 20000208 US

non-provisional-of-provisional 60224596 20000811 US

non-provisional-of-provisional 60181004 20000208 US

non-provisional-of-provisional 60180930 20000208 US

US-CL-CURRENT: 514/12, 435/189 , 435/320.1 , 435/325 , 435/69.1 , 536/23.2

ABSTRACT:

The present invention provides novel isolated NOVX polynucleotides and polypeptides encoded by the NOVX polynucleotides. Also provided are the antibodies that immunospecifically bind to a NOVX polypeptide or any derivative, variant, mutant or fragment of the NOVX polypeptide, polynucleotide or antibody. The invention additionally provides methods in which the NOVX polypeptide, polynucleotide and antibody are utilized in the detection and treatment of a broad range of pathological states, as well as to other uses.

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Ser. No. 60/180,646, filed Feb. 7, 2000; U.S. Ser. No. 60/220,262, filed Jul. 24, 2000; U.S. Ser. No. 60/245,292, filed Nov. 2, 2000; U.S. Ser. No. 60/180,511, filed Feb. 7, 2000; U.S. Ser. No. 60/180,630, filed Feb. 7, 2000; U.S. Ser. No. 60/220,594, filed Jul. 25, 2000; U.S. Ser. No. 60/181,013, filed Feb. 8, 2000; U.S. Ser. No. 60/181,043, filed Feb. 8, 2000; U.S. Ser. No. 60/224,596, filed Aug. 11, 2000; U.S. Ser. No. 60/181,004, filed Feb. 8, 2000; and U.S. Ser. No. 60/180,930, filed Feb. 8, 2000 which are incorporated herein by reference in their entirety.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (33):

[0030] Issel-Tarver and Rine (1996) characterized 4 members of the canine olfactory receptor gene family. The 4 subfamilies comprised genes expressed exclusively in olfactory epithelium. Analysis of large DNA fragments using Southern blots of pulsed field gels indicated that subfamily members were clustered together, and that two of the subfamilies were closely linked in the dog genome. Analysis of the four olfactory receptor gene subfamilies in 26 breeds of dog provided evidence that the number of genes per subfamily was stable in spite of differential selection on the basis of olfactory acuity in scent hounds, sight hounds, and toy breeds.

Summary of Invention Paragraph - BSTX (717):

[0714] In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to a NOVX protein determined. The cell, for example, can be of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the NOVX protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the NOVX protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with .sup.125I, .sup.35S, .sup.14C, or .sup.3H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds NOVX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a NOVX protein, wherein determining the ability of the test compound to interact with a NOVX protein comprises determining the ability of the test compound to preferentially bind to NOVX protein or a biologically-active portion thereof as compared to the known compound.

Summary of Invention Paragraph - BSTX (719):

[0716] Determining the ability of the NOVX protein to bind to or interact with a NOVX target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment; determining the

ability of the NOVX protein to bind to or interact with a NOVX target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (i.e. intracellular Ca.sup.2+, diacylglycerol, IP.sub.3, etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the induction of a reporter gene (comprising a NOVX-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, e.g., luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

Summary of Invention Paragraph - BSTX (746):

[0743] An antibody specific for a protein of the invention can be used to isolate the protein by standard techniques, such as immunoaffinity chromatography or immunoprecipitation. Such an antibody can facilitate the purification of the natural protein antigen from cells and of recombinantly produced antigen expressed in host cells. Moreover, such an antibody can be used to detect the antigenic protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the antigenic protein. Antibodies directed against the protein can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, .beta.-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include .sup.125I, .sup.131I, .sup.35S or .sup.3H.

PGPUB-DOCUMENT-NUMBER: 20030082174

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030082174 A1

TITLE: Novel proteins and nucleic acids encoding same

PUBLICATION-DATE: May 1, 2003

INVENTOR-INFORMATION:

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Smithson, Glennda	Guilford	CT	US	

APPL-NO: 09/ 864029

DATE FILED: May 23, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60207020 20000525 US

non-provisional-of-provisional 60219786 20000719 US

non-provisional-of-provisional 60220593 20000725 US

non-provisional-of-provisional 60239542 20001010 US

non-provisional-of-provisional 60275590 20010313 US

non-provisional-of-provisional 60256402 20001218 US

non-provisional-of-provisional 60274809 20010309 US

non-provisional-of-provisional 60206757 20000524 US

non-provisional-of-provisional 60271645 20010226 US

non-provisional-of-provisional 60214372 20000628 US

US-CL-CURRENT: 424/143.1, 435/320.1 , 435/325 , 435/69.1 , 530/350 , 536/23.5

ABSTRACT:

Disclosed herein are nucleic acid sequences that encode G-coupled protein-receptor related polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivatives, variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

RELATED APPLICATIONS

[0001] This application claims priority from Provisional Applications U.S. Pat. No. 60/207020, filed May 25, 2000; U.S. Pat. No. 60/219,786, filed Jul. 19, 2000; U.S. Pat. No. 60/220,593, filed Jul. 25, 2000; U.S. Pat. No. 60/239,542, filed Oct. 10, 2000; U.S. Pat. No. 60/275,590, filed Mar. 13, 2001; U.S. Pat. No. 60/256,402, filed Dec. 18, 2000; U.S. Pat. No. 60/274,809, filed Mar. 9, 2001; U.S. Pat. No. 60/206,757, filed May 24, 2000; U.S. Pat. No. 60/271,645, filed Feb. 26, 2001; and U.S. Pat. No. 60/214,372, filed Jun. 28, 2000, each of which is incorporated by reference in its entirety.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (38):

[0035] Issel-Tarver and Rine (1996) characterized 4 members of the canine olfactory receptor gene family. The 4 subfamilies comprised genes expressed exclusively in olfactory epithelium. Analysis of large DNA fragments using Southern blots of pulsed field gels indicated that subfamily members were clustered together, and that two of the subfamilies were closely linked in the dog genome. Analysis of the four olfactory receptor gene subfamilies in 26 breeds of dog provided evidence that the number of genes per subfamily was stable in spite of differential selection on the basis of olfactory acuity in scent hounds, sight hounds, and toy breeds.

Summary of Invention Paragraph - BSTX (230):

[0198] An anti-GPCRX antibody (e.g., monoclonal antibody) can be used to isolate an GPCRX polypeptide by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-GPCRX antibody can facilitate the purification of natural GPCRX polypeptide from cells and of recombinantly-produced GPCRX polypeptide expressed in host cells. Moreover, an anti-GPCRX antibody can be used to detect GPCRX protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the GPCRX protein. Anti-GPCRX antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, .beta.-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent

materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include .sup.125I, .sup.131I, .sup.35S or .sup.3H.

Summary of Invention Paragraph - BSTX (279):

[0242] In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of GPCRX protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to an GPCRX protein determined. The cell, for example, can of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the GPCRX protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the GPCRX protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with .sup.125I, .sup.35S, .sup.14C, or .sup.3H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of GPCRX protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds GPCRX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an GPCRX protein, wherein determining the ability of the test compound to interact with an GPCRX protein comprises determining the ability of the test compound to preferentially bind to GPCRX protein or a biologically-active portion thereof as compared to the known compound.

Summary of Invention Paragraph - BSTX (281):

[0244] Determining the ability of the GPCRX protein to bind to or interact with an GPCRX target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the ability of the GPCRX protein to bind to or interact with an GPCRX target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (i.e. intracellular Ca.sup.2+, diacylglycerol, IP.sub.3, etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the induction of a reporter gene (comprising an GPCRX-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, e.g., luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

PGPUB-DOCUMENT-NUMBER: 20030077794

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030077794 A1

TITLE: Novel polypeptides and nucleic acids encoding same

PUBLICATION-DATE: April 24, 2003

INVENTOR-INFORMATION:

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APPL-NO: 09/ 898586

DATE FILED: July 3, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60177839 20000125 US

non-provisional-of-provisional 60176134 20000114 US

non-provisional-of-provisional 60175989 20000113 US

non-provisional-of-provisional 60218324 20000714 US

non-provisional-of-provisional 60220253 20000724 US

non-provisional-of-provisional 60178191 20000126 US

non-provisional-of-provisional 60178227 20000126 US

non-provisional-of-provisional 60220590 20000725 US

non-provisional-of-provisional 60215855 20000703 US

US-CL-CURRENT: 435/189, 435/320.1 , 435/325 , 435/6 , 435/69.1 , 536/23.2

ABSTRACT:

The present invention provides novel isolated NOVX polynucleotides and polypeptides encoded by the NOVX polynucleotides. Also provided are the antibodies that immunospecifically bind to a NOVX polypeptide or any derivative, variant, mutant or fragment of the NOVX polypeptide, polynucleotide or antibody. The invention additionally provides methods in which the NOVX polypeptide, polynucleotide and antibody are utilized in the detection and treatment of a broad range of pathological states, as well as to other uses.

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Ser. No. 60/177,839, filed Jan. 25, 2000; U.S. Ser. No. 60/176,134, filed Jan. 14, 2000; U.S. Ser. No. 60/175,989, filed Jan. 13, 2000; U.S. Ser. No. 60/218,324, filed Jul. 14, 2000; U.S. Ser. No. 60/220,253, filed Jul. 24, 2000; U.S. Ser. No.

60/178,191, filed Jan. 26, 2000; U.S. Ser. No. 60/178,227, filed Jan. 26, 2000; U.S. Ser. No. 60/220,590, filed Jul. 25, 2000, U.S. Ser. No. 60/215,855 (21402-048) filed Jul. 3, 2000, and U.S. Ser. No. 09/761,288 (15966-638 utility) filed Jan. 16, 2001, which are incorporated herein by reference in their entirety.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (33):

[0030] Issel-Tarver and Rine (1996) characterized 4 members of the canine olfactory receptor gene family. The 4 subfamilies comprised genes expressed exclusively in olfactory epithelium. Analysis of large DNA fragments using Southern blots of pulsed field gels indicated that subfamily members were clustered together, and that two of the subfamilies were closely linked in the dog genome. Analysis of the four olfactory receptor gene subfamilies in 26 breeds of dog provided evidence that the number of genes per subfamily was stable in spite of differential selection on the basis of olfactory acuity in scent hounds, sight hounds, and toy breeds.

Summary of Invention Paragraph - BSTX (338):

[0335] In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to a NOVX protein determined. The cell, for example, can be of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the NOVX protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the NOVX protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with .sup.125I, .sup.35S, .sup.14C, or .sup.3H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds NOVX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a NOVX protein, wherein determining the ability of the test compound to interact with a NOVX protein comprises determining the ability of the test compound to preferentially bind to NOVX protein or a biologically-active portion thereof as compared to the known compound.

Summary of Invention Paragraph - BSTX (340):

[0337] Determining the ability of the NOVX protein to bind to or interact with a NOVX target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the ability of the NOVX protein to bind to or interact with a NOVX target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (i.e. intracellular Ca.sup.2+, diacylglycerol, IP.sub.3, etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the induction of a reporter gene (comprising a NOVX-responsive regulatory element operatively

linked to a nucleic acid encoding a detectable marker, e.g., luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

Summary of Invention Paragraph - BSTX (366):

[0363] An antibody specific for a protein of the invention can be used to isolate the protein by standard techniques, such as immunoaffinity chromatography or immunoprecipitation. Such an antibody can facilitate the purification of the natural protein antigen from cells and of recombinantly produced antigen expressed in host cells. Moreover, such an antibody can be used to detect the antigenic protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the antigenic protein. Antibodies directed against the protein can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, .beta.-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include .sup.125I, .sup.131I, .sup.35S or .sup.3H.

PGPUB-DOCUMENT-NUMBER: 20030059830

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030059830 A1

TITLE: Novel single nucleotide polymorphisms for olfactory receptor-like polypeptides and nucleic acids encoding the same

PUBLICATION-DATE: March 27, 2003

INVENTOR-INFORMATION:

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APPL-NO: 09/ 974591

DATE FILED: October 9, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60245292 20001102 US

US-CL-CURRENT: 435/7.1, 435/320.1 , 435/325 , 435/6 , 435/69.1 , 530/350 , 536/23.5

ABSTRACT:

The present invention provides novel nucleic acid sequences having single nucleotide polymorphisms that encode olfactory receptor-like polypeptides and the polypeptides so encoded. Also provided are the antibodies that immunospecifically bind to these polypetides or any derivative, variant,mutant or fragment of the polypeptide, polynucleotide or antibody. The invention additionally provides methods in which the polypetide, polynucleotide and antibody are utilized in the detection and treatment of a broad range of pathological states, as well as to uses.

RELATED APPLICATIONS

[0001] This application claims the benefit of priority to Provisional Application U.S. Serial No. 60/_____ , filed Sep. 20, 2001; U.S. Ser. No. 09/777,789, filed Feb. 6, 2001; and U.S. Ser. No. 60/245,292, filed Nov. 2, 2000; each of which is incorporated herein by reference in its entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (6):

[0028] Issel-Tarver and Rine characterized 4 members of the canine olfactory receptor gene isle family (Issel-Tarver and Rine, "Organization and expression of canine olfactory genes," 93(20) PNAS. USA 10897-902 (Oct. 1, 1996)). The 4 subfamilies comprised genes expressed exclusively in olfactory epithelium.

Analysis of large DNA fragments using Southern blots of pulsed field gels indicated that subfamily members were clustered together, and that two of the subfamilies were closely linked in the dog genome. Analysis of the four olfactory receptor gene subfamilies in 26 breeds of dog provided evidence that the number of genes per subfamily was stable in spite of differential selection on the basis of olfactory acuity in scent hounds, sight hounds. and toy breeds.

Detail Description Paragraph - DETX (267):

[0289] In brief, pyrosequencing is a real time primer extension process of genotyping. This protocol takes double-stranded, biotinylated PCR products from genomic DNA samples and binds them to streptavidin beads. These beads are then denatured producing single stranded bound DNA. SNPs are characterized utilizing a technique based on an indirect bioluminometric assay of pyrophosphate (PPi) that is released from each dNTP upon DNA chain elongation. Following Klenow polymerase-mediated base incorporation, PPi is released and used as a substrate, together with adenosine 5' -phosphosulfate (APS), for ATP sulfurylase, which results in the formation of ATP. Subsequently, the ATP accomplishes the conversion of luciferin to its oxi-derivative by the action of luciferase. The ensuing light output becomes proportional to the number of added bases, up to about four bases. To allow processivity of the method dNTP excess is degraded by apyrase, which is also present in the starting reaction mixture, so that only dNTPs are added to the template during the sequencing. The process has been fully automated and adapted to a 96-well format, which allows rapid screening of large SNP panels.

Detail Description Paragraph - DETX (383):

[0405] In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to a NOVX protein determined. The cell, for example, can be of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the NOVX protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the NOVX protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with .sup.125I, .sup.35S, .sup.14C, or .sup.3H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds NOVX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a NOVX protein, wherein determining the ability of the test compound to interact with a NOVX protein comprises determining the ability of the test compound to preferentially bind to NOVX protein or a biologically-active portion thereof as compared to the known compound.

Detail Description Paragraph - DETX (385):

[0407] Determining the ability of the NOVX protein to bind to or interact with a NOVX target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the

ability of the NOVX protein to bind to or interact with a NOVX target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (i e intracellular Ca.sup.2+, diacylglycerol, IP.sub.3, etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the induction of a reporter gene (comprising a NOVX-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, e.g., luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

Detail Description Paragraph - DETX (411):

[0433] An antibody specific for a protein of the invention can be used to isolate the protein by standard techniques, such as immunoaffinity chromatography or immunoprecipitation. Such an antibody can facilitate the purification of the natural protein antigen from cells and of recombinantly produced antigen expressed in host cells. Moreover, such an antibody can be used to detect the antigenic protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the antigenic protein. Antibodies directed against the protein can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes. prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, .beta.-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include .sup.125I, .sup.131I, .sup.35S or .sup.3H.

US-PAT-NO: 6630153

DOCUMENT-IDENTIFIER: US 6630153 B2

TITLE: Manufacture of bone graft substitutes

DATE-ISSUED: October 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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Schryver; Jeff	Cordova	TN	N/A	N/A

APPL-NO: 09/ 792681

DATE FILED: February 23, 2001

US-CL-CURRENT: 424/422, 424/423 , 424/426 , 424/484 , 424/501

ABSTRACT:

The present invention is directed to methods and compositions for manufacturing a bone graft substitute. A powder compaction process is utilized to generate a shaped product comprised of a granulated bone material, such as demineralized bone matrix. In addition, a processing aid is utilized to facilitate compaction of the granulated bone material and for release of the product from the die.

33 Claims, 6 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 6

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Detailed Description Text - DETX (14):
The term "JAX.TM." as used herein is defined as a bone graft substitute particle which generally has the shape of a toy jack. In a specific embodiment, it is a three-dimensional six-armed star shape.

Detailed Description Text - DETX (31):
In a specific embodiment, the bone material of the present invention is colored to make it more visible. In another specific embodiment, differently shaped BGS of the present invention are denoted with different colors for better differentiation of the particles. In another specific embodiment, the particles are coated or have contained within them an agent such as green fluorescent protein or blue fluorescent protein to make them fluorescent and therefore more visible.

Claims Text - CLTX (32):

32. The method of claim 1, wherein said shape generally has the shape of a toy jack.

US-PAT-NO: 6572244

DOCUMENT-IDENTIFIER: US 6572244 B1

TITLE: Novelty item having illuminating handle

DATE-ISSUED: June 3, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Clark; Jim	Tulsa	OK	74133	N/A

APPL-NO: 10/ 034577

DATE FILED: December 27, 2001

PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATIONS

This is a continuation application of Ser. No. 09/480,028 filed on Jan. 10, 2000 abandoned.

US-CL-CURRENT: 362/253, 362/109 , 362/34 , 362/806 , 362/84

ABSTRACT:

The present invention is directed to an illuminated novelty item. In one embodiment, the novelty item includes an edible, food item supported on a hollow, translucent handle. A light source is also provided to illuminate the interior, hollow portion of the handle. Since the handle is translucent, the light radiated through the handle and into the edible food item. If the food item is translucent, which it preferable is, then the light also radiates through the food item in a unique and visually-desirable fashion. In one embodiment the food item is an ice confection, such as a Popsicle.RTM. Ice Confection. In another embodiment, the food item may be cotton candy. In yet another embodiment, the food item may be a sucker or lollipop, which is supported on a translucent handle in the same way as the ice confection mentioned above. Consistent with the invention, the light source may take on a variety of forms. In one embodiment, the light source may be a simple incandescent light that may be, for example, battery operated. Preferably, however, the light source is a passive (i.e., not requiring a battery or other power source) component, such as a bioluminescent or phosphorescent material. In the preferred embodiment, the light source may be a material such as a Glow Stick, Glow Worm, or other such device that is commonly sold at amusement parks.

11 Claims, 5 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 4

---------- KWIC ---------

Abstract Text - ABTX (1):

The present invention is directed to an illuminated novelty item. In one embodiment, the novelty item includes an edible, food item supported on a hollow, translucent handle. A light source is also provided to illuminate the interior, hollow portion of the handle. Since the handle is translucent, the light radiated through the handle and into the edible food item. If the food item is translucent, which it preferable is, then the light also radiates through the food item in a unique and visually-desirable fashion. In one embodiment the food item is an ice confection, such as a Popsicle.RTM. Ice Confection. In another embodiment, the food item may be cotton candy. In yet another embodiment, the food item may be a sucker or lollipop, which is supported on a translucent handle in the same way as the ice confection mentioned above. Consistent with the invention, the light source may take on a variety of forms. In one embodiment, the light source may be a simple incandescent light that may be, for example, battery operated. Preferably, however, the light source is a passive (i.e., not requiring a battery or other power source) component, such as a bioluminescent or phosphorescent material. In the preferred embodiment, the light source may be a material such as a Glow Stick, Glow Worm, or other such device that is commonly sold at amusement parks.

Brief Summary Text - BSTX (9):

Many such items have been the subject of U.S. patents. For example, U.S. Pat. No. 5,946,773 is directed to a food product having a uniquely shaped and multi-colored handle. U.S. Pat. No. 5,939,983 discloses a novelty device that makes a sound and/or illuminates a light as a user is consuming (or otherwise comes in contact with) a consumable substance supported on a handle of the device. U.S. Pat. No. 5,666,693 discloses a unique toy handle for an oral device, such as a lollipop or popsicle. Specifically, FIGS. 1A-1C of that patent illustrate a handle in the shape of the back end of an animal, like a lizard or a frog. This uniquely-shaped handle gives the appearance of the consumer eating a frog or lizard, when the consumable end of the product is held in the mouth of the consumer.

Brief Summary Text - BSTX (19):

Consistent with the invention, the light source may take on a variety of forms. In one embodiment, the light source may be a simple incandescent light that may be, for example, battery operated. Preferably, however, the light source is a passive (i.e., not requiring a battery or other power source) component, such as a bioluminescent or phosphorescent material. In the preferred embodiment, the light source may be a material such as a Glow Stick, Glow Worm, or other such device that is commonly sold at amusement parks. The handle of the novelty item may be a hollow, cylindrically-shaped handle appropriately sized such that a Glow Stick, Glow Worm, or other similar device may be inserted into the hollow space of the handle. In this way, the light that radiates from the light source radiates through the translucent handle and through the edible food item.

Detailed Description Text - DETX (7):

Consistent with the invention, the light source 106 may take on a variety of forms. In one embodiment, the light source 106 may be a simple incandescent light that may be, for example, battery operated. Preferably, however, the light source is a passive (i.e., not requiring a battery or other power source) component, such as a bioluminescent or phosphorescent material. In the preferred embodiment, the light source 106 may be a device such as a Glow Stick, Glow Worm, or other such device that is commonly sold at amusement parks. The handle of the novelty item 100 may include a hollow,

cylindrically-shaped handle 104 appropriately sized such that a Glow Stick, Glow Worm, or other similar device may be inserted into the hollow space of the handle 104. In this way, the light that radiates from the light source 106 radiates through the translucent handle 104 and through the edible food item 102.

Detailed Description Text - DETX (8):
Thus, one embodiment, the light source 106 may be a phosphorescent light source. Phosphorescent amusement devices, including so-called "glow-in-the-dark" toys, have been popular for a long time. As is well known, many different interesting glow-in-the-dark effects can be achieved by incorporating phosphorescent chemicals into a myriad of different toy configurations. For example, U.S. Pat. No. 2,644,890, which is hereby incorporated by reference, discloses amusement devices, each of which consists of a sealed envelope containing phosphorescent particles visible from outside the envelope. Other materials and types of phosphorescent devices may be utilized to provide the light source 106 of the present invention. U.S. Pat. No. 5,830,034, which is hereby incorporated by reference, also discloses a phosphorescent amusement device. Since phosphorescent devices are well known, the details of implementing such a device or quality as the light source of one embodiment of the present invention need not be described herein.

Detailed Description Text - DETX (9):
As an alternative to the above-disclosed light sources, the light source 106 may also be in the form of a bioluminescent material. As is known, luminescence is a phenomenon in which energy is specifically channeled to a molecule to produce an excited state. Return to a lower energy state is accompanied by release of a photon. Luminescence includes fluorescence, phosphorescence, chemiluminescence and bioluminescence. Bioluminescence is the process by which living organisms emit light that is visible to other organisms. When the luminescence is bioluminescence, creation of the excited state derives from an enzyme catalyzed reaction. The color of the emitted light in a bioluminescent (or chemiluminescent or other luminescent) reaction is characteristic of the excited molecule, and is independent from its source of excitation and temperature.

Detailed Description Text - DETX (10):
An important condition for bioluminescence is the use of molecular oxygen, either bound or free in the presence of a luciferase. Luciferases, are oxygenases, that act on a substrate, luciferin, in the presence of molecular oxygen and transform the substrate to an excited state. Upon return to a lower energy level, energy is released in the form of light.

Detailed Description Text - DETX (11):
Bioluminescence, as well as other types of chemiluminescence, may be used for quantitative determinations of specific substances in biology and medicine. For example, luciferase genes have been cloned and exploited as reporter genes in numerous assays, for many purposes. Since the different luciferase systems have different specific requirements, they may be used to detect and quantify a variety of substances. The majority of commercial bioluminescence applications are based on firefly.

Detailed Description Text - DETX (12):
Bioluminescence may also be used as the light source 106 of the invention,

because it can be sustained to provide a glow that lasts, if desired, from minutes up to hours. As yet an alternative light source, a laser could be used be used to provide the light source 106 of the invention.

Claims Text - CLTX (7):
7. The novelty food item of claim 1 wherein the light source is a **bioluminescent** material.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	23151	bioluminesc$ or fluorescen$ near4 protein$1 or luciferase$1 or photoprotein$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:40
L2	152305	bubble$	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:41
L3	24	1 same 2	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:42
L4	83381	toy or novelty	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:43
L5	46	1 and 2 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L6	28	1 same 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L7	40	1 and toy	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:45
L9	27	7 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L10	34	1 and novelty adj item$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 12:00
L11	18	10 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L12	286	((chemilumines$ or lumines$8 or glow$8) same 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:28
L13	29	((chemilumines$ or lumines$8 or glow$8) near4 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:28

PGPUB-DOCUMENT-NUMBER: 20030164105

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030164105 A1

TITLE: Lithographic printing plate precursor

PUBLICATION-DATE: September 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Tashiro, Hiroshi	Shizuoka		JP	

APPL-NO: 10/ 370694

DATE FILED: February 24, 2003

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
JP	P.2002-048052	2002JP-P.2002-048052	February 25, 2002
JP	P.2002-191051	2002JP-P.2002-191051	June 28, 2002

US-CL-CURRENT: 101/453

ABSTRACT:

A lithographic printing plate precursor of the present invention comprises a water-resistant support, a hydrophilic layer and an image-forming layer, in this order, said hydrophilic layer comprising a fine particulate hydrophobicizing precursor and a hydrophilic binder polymer, and said image forming layer comprising a light-heat converting substance and a microcapsule encapsulating a hydrophobic substance, wherein the hydrophilic binder polymer is a composite material of a hydrophilic organic polymer and a polymer having a group including: at least one atom selected from a metal atom and semimetal atom; and an oxygen atom connecting with the at least one atom selected from a metal atom and semimetal atom.

---------- KWIC ---------

Detail Description Paragraph - DETX (25):

[0333] Then, the glow-treated film was immersed in a nitrogen bubbled aqueous acrylic acid solution (20%) at 60.degree. C. for 4 hours. After the immersion, the film was washed with running water for 10 minutes to obtain Support S having a hydrophilic layer which surface was graft polymerized with an acrylic acid.

PGPUB-DOCUMENT-NUMBER: 20030157346

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030157346 A1

TITLE: Gas Barrier film

PUBLICATION-DATE: August 21, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kawamura, Koichi	Shizuoka-ken		JP	
Kano, Takeyoshi	Shizuoka-ken		JP	
Takahashi, Miki	Shizuoka-ken		JP	

APPL-NO: 10/ 366381

DATE FILED: February 14, 2003

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
JP	2002-036676	2002JP-2002-036676	February 14, 2002
JP	2002-241739	2002JP-2002-241739	August 22, 2002

US-CL-CURRENT: 428/451, 428/500 , 428/520

ABSTRACT:

The invention provides a gas barrier film having a support including a hydrophilic surface or a non-ionic hydrophobic surface on which a graft polymer chain having a polar group is present, and an inorganic thin film formed on the surface.

---------- KWIC ---------

Detail Description Paragraph - DETX (7):

[0076] The resultant film, which had been subjected to the glow treatment, was immersed in a nitrogen-bubbled aqueous solution of sodium styrenesulfonate (10 wt %) at 70.degree. C. for 7 hours. After the immersion, the film was washed with water for 8 hours to prepare a support (support A) in which sodium styrenesulfonate was graft-polymerized on the surface thereof.

PGPUB-DOCUMENT-NUMBER: 20030155560

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030155560 A1

TITLE: Formable, porous, chemiluminescent reactant composition and device therefor

PUBLICATION-DATE: August 21, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Palmer, William R.	Rescue	CA	US	
Palmer, Stephen L.	Cameron Park	CA	US	
Cranor, Earl	Longmeadow	MA	US	

APPL-NO: 10/ 076051

DATE FILED: February 12, 2002

US-CL-CURRENT: 252/700

ABSTRACT:

A formable, porous chemiluminescent reactant composition, device therefore, and a process for production thereof is disclosed. The fluidizable solid admixture of the instant invention may be cured to a more or less rigid form with or without the use of a mold. The cured solid is useful as a chemiluminescent reactant component and is useful in a variety of environments.

---------- KWIC ---------

Detail Description Paragraph - DETX (6):

[0046] Previous attempts at producing these "candles" which use chemiluminescent systems as light sources have met with drawbacks. Typically, a chemiluminescent lighting device, such as a light stick, which employs liquids, has a head-space in the device which represents approximately 30% of the container volume. Light cannot be produced in this head-space area. Japanese Pat. Application No. 10-170263 discloses an air bubble capture means in which the gaseous head-space (or bubble) which is above the liquid chemiluminescent fluid in a sealed chemiluminescent device is trapped in a region of the device other than the uppermost portion. By displacing the bubble from the upper tip portion of a sealed chemiluminescent device, such as a candle for example, the entire portion of the candle flame tip will appear to glow during the chemiluminescent reaction. If the bubble had been permitted to remain at the flame tip, it would create a dark region near the top of the flame since the area of the bubble will not produce any light. Such a dark region would detract from the overall visual acceptability of the device. Carbon dioxide, carbon monoxide, and oxygen are common gases liberated in peroxyluminescent systems. These gases rise to the top of any liquid chemiluminescent system and form bubbles at the top of the device. Thus, while the device described in Japanese Pat. Application No. 10-170263 may effectively eliminate the problem of bubbles initially contained at the top of a chemiluminescent device, a method is not provided to displace bubbles which are generated during the chemiluminescent process. The instant invention permits a candle or any other chemiluminescent object desired to be produced in

which an initial head-space bubble in the device and any significant visible build up of bubbles in the device as the chemiluminescent process progresses is eliminated. In addition, the instant invention does not require any specially formed traps, channels, or valves in the device to realize this benefit. Since the formable mass of the chemiluminescent system of the instant invention is a solid, there is no space for bubbles to aggregate and combine. While gasses generated during the chemiluminescent process are still produced, these gasses are constrained from rising in the solid formable mass and are evenly distributed throughout the solid, which subsequently result in a seemingly flawless output of light.

PGPUB-DOCUMENT-NUMBER: 20030147303

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030147303 A1

TITLE: Cavitation mixer

PUBLICATION-DATE: August 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Schueler, Rolf	Worth		DE	

APPL-NO: 10/ 220097

DATE FILED: December 30, 2002

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	100 09 326.4	2000DE-100 09 326.4	February 28, 2000

PCT-DATA:
APPL-NO: PCT/EP01/02253
DATE-FILED: Feb 28, 2001
PUB-NO:
PUB-DATE:
371-DATE:
102(E)-DATE:

US-CL-CURRENT: 366/176.2

ABSTRACT:

A device for mixing the components of a mass flow flowing through the same provides a particularly homogenous mixture which remains stable for any length of time, even when the components concerned are generally not miscible or are very difficult to mix. The device has a body (8) which is located in a throughflow chamber (4) and is difficult to flow around. This body is situated at least partially in a part of the throughflow chamber (4) that expands in the direction of the flow, so that the cavitation effect and the mixing effect of the supercavitation field produced by the body (8) that is hard to flow around are considerably amplified.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (9):

[0008] The examples mentioned above relate to cavitation which occurs in the flow field or in the acoustic field as a result of a tensile stress which is present in the water or a liquid. Generating a further type of cavitation involves locally depositing energy in the liquid, for example by means of a spark or a laser pulse. Details of the latter are to be found, for example in the thesis written by Olgert Lindau, "Dynamik und Lumineszenz lasererzeugter Kavitationsblasen", [Dynamics and luminescence of laser-generated cavitation bubbles], 1998, written at the Third Physics Institute of the Georg-August-Universitt in Gottingen.

PGPUB-DOCUMENT-NUMBER: 20030143592

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030143592 A1

TITLE: DNA chip

PUBLICATION-DATE: July 31, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kawamura, Koichi	Shizuoka-ken		JP	
Makino, Yoshihiko	Saitama-ken		JP	
Takahashi, Miki	Shizuoka-ken		JP	

APPL-NO: 10/ 278083

DATE FILED: October 23, 2002

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
JP	2001-327569	2001JP-2001-327569	October 25, 2001
JP	2001-329170	2001JP-2001-329170	October 26, 2001

US-CL-CURRENT: 435/6, 435/287.2

ABSTRACT:

The present invention provides a DNA chip including: a solid support having a surface; a DNA fragment immobilized on the surface; and a graft polymer bonded to the surface, wherein the DNA fragment is immobilized on the surface via the graft polymer. The invention also provides a DNA chip including: a solid support made of a resinous material and having a surface; a DNA fragment immobilized on the surface; and a graft polymer bonded to the surface, wherein the DNA fragment is immobilized on the surface via the graft polymer.

---------- KWIC ---------

Detail Description Paragraph - DETX (72):

[0086] The film, which had been subjected to the glow treatment, was immersed in a nitrogen bubbled solution (10 wt %) of acrylic acid at 70.degree. C. for 7 hours. After the immersion, the film was washed with water for 8 hours to thereby prepare a solid support (solid support 1) in which acrylic acid was graft-polymerized on the surface thereof.

PGPUB-DOCUMENT-NUMBER: 20030052951

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030052951 A1

TITLE: Ink jet recording apparatus using recording unit with ink cartridge having ink inducing element

PUBLICATION-DATE: March 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ujita, Toshihiko	Kanagawa		JP	
Takenouchi, Masanori	Kanagawa		JP	
Tsukuda, Keiichiro	Kanagawa		JP	

APPL-NO: 10/ 223363

DATE FILED: August 20, 2002

RELATED-US-APPL-DATA:

child 10223363 A1 20020820

parent division-of 09016322 19980130 US GRANTED

parent-patent 6454399 US

child 09016322 19980130 US

parent division-of 08669644 19960624 US GRANTED

parent-patent 5784088 US

child 08669644 19960624 US

parent continuation-of 08165843 19931214 US ABANDONED

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
JP	179,195/1993	1993JP-179,195/1993	July 20, 1993
JP	298,370/1993	1993JP-298,370/1993	November 29, 1993
JP	298,500/1993	1993JP-298,500/1993	November 29, 1993
JP	298,501/1993	1993JP-298,501/1993	November 29, 1993

US-CL-CURRENT: 347/86

ABSTRACT:

An ink cartridge (3) including an ink reservoir portion having a porous member (37) for storing ink and an ink supply portion (39) has an ink inducing element (47) disposed between the ink reservoir portion and the ink supply portion (39). The ink inducing element (47) is made of bundle of fibers in which each fiber is disposed in parallel to the direction of ink supplying from the ink reservoir to the ink supply portion (39), and one end of the ink inducing element (47) is press-touched to the porous member (37).

---------- KWIC ---------

Detail Description Paragraph - DETX (98):

[0199] However, occasionally a size of the air **bubbles become glowing** within the period described above under a bad environmental condition such as under both an extremely high temperature and a low relative humidity, and these grown air bubbles interrupt the ink flow to the recording head to cause its poor printing abilities. Especially in case of that the valve mechanism 614 is driven at the time of connecting or separating the ink-jet recording head 602 and the ink cartridge 601 as shown in FIG. 8A, the air from the outside may be introduced into a certain region of the ink path, which corresponds to an extent of the valve movement or the like. Therefore, the valve mechanism makes an unfavorable condition under the environment described above.

PGPUB-DOCUMENT-NUMBER: 20030052011

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030052011 A1

TITLE: Plasma electroplating

PUBLICATION-DATE: March 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Chen, Zhuping	Beijing		CN	

APPL-NO: 10/ 130582

DATE FILED: September 10, 2002

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
AU	PR 1299	2000AU-PR 1299	November 8, 2000

PCT-DATA:
APPL-NO: PCT/AU01/01435
DATE-FILED: Nov 8, 2001
PUB-NO:
PUB-DATE:
371-DATE:
102(E)-DATE:

US-CL-CURRENT: 205/80, 205/148 , 422/186.04

ABSTRACT:

A method for depositing a film of an advanced material on a surface of an article is disclosed. The method comprises placing the article within a bath having a pair of spaced electrodes one of which is formed by said article and an electrolyte containing a source of the material to be deposited. A stream of bubbles is generated within the electrolyte adjacent to the cathode. There are a number of techniques for generating the stream of bubbles, e.g. electrolysis, ebullition, cavitation, entrainment and sparging. The method also includes applying a potential difference across the cathode and anode such that a glow discharge is formed in the bubble region so as form a plasma of ionised gaseous molecules within the bubble. This highly energised gaseous plasma then acts to deposit a film of material on the surface of the article. The method may be carried out at atmospheric pressure and does not require a vacuum apparatus. The body of electrolyte liquid acts as a source of containment for the plasma. In large potential difference or voltage drop across the stream of bubbles facilitates the formation of a glow discharge in this region which energises and ionises the molecules to be deposited. An apparatus for carrying out this method is also disclosed.

---------- KWIC ---------

Abstract Paragraph - ABTX (1):
A method for depositing a film of an advanced material on a surface of an

article is disclosed. The method comprises placing the article within a bath having a pair of spaced electrodes one of which is formed by said article and an electrolyte containing a source of the material to be deposited. A stream of bubbles is generated within the electrolyte adjacent to the cathode. There are a number of techniques for generating the stream of bubbles, e.g. electrolysis, ebullition, cavitation, entrainment and sparging. The method also includes applying a potential difference across the cathode and anode such that a glow discharge is formed in the bubble region so as form a plasma of ionised gaseous molecules within the bubble. This highly energised gaseous plasma then acts to deposit a film of material on the surface of the article. The method may be carried out at atmospheric pressure and does not require a vacuum apparatus. The body of electrolyte liquid acts as a source of containment for the plasma. In large potential difference or voltage drop across the stream of bubbles facilitates the formation of a glow discharge in this region which energises and ionises the molecules to be deposited. An apparatus for carrying out this method is also disclosed.

Summary of Invention Paragraph - BSTX (23):

[0019] applying a potential difference across the cathode and anode such that a glow discharge is formed in the bubble region so as to form a plasma of ionised gaseous molecules within the bubbles;

Summary of Invention Paragraph - BSTX (36):

[0032] The step of forming a glow discharge in the bubble region may be achieved by increasing the potential difference across the electrodes above a specified point.

Summary of Invention Paragraph - BSTX (73):

[0069] In essence the process described above provides both a technique for the deposition of advanced materials as well as a convenient alternative plating system to conventional electroplating techniques. The essence of the process resides in inducing a state of non-equilibrium in a precursor material contained in a sheath of bubbles adjacent an electrode to provide the energy and velocity to effect efficacious deposition. This is achieved by applying an electric field of sufficient strength generate a plasma glow discharge in the bubbles. The ionised and energised ions are then deposited and bonded to the surface at a very high but localised temperature.

Claims Text - CLTX (1):

1. A method for depositing a material on a surface of an article, comprising: providing a bath containing an electrolyte and a pair of spaced electrodes whereby one electrode forms the article; generating within the electrolyte a stream of bubbles which contain a source of the material to be deposited so as to form a bubble region around the electrode forming the article; applying a potential difference across the electrodes such that a plasma glow discharge is formed in the bubble region and said material is plasma deposited on said article.

US-PAT-NO: 6613455

DOCUMENT-IDENTIFIER: US 6613455 B1

TITLE: Electroluminescent device and method for producing same

DATE-ISSUED: September 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Matsumoto; Kazumi	Sagamihara	N/A	N/A	JP
Kobayashi; Mitsuaki	Tokyo	N/A	N/A	JP
Araki; Yoshinori	Sagae	N/A	N/A	JP
Abe; Hidetoshi	Tendo	N/A	N/A	JP

APPL-NO: 09/ 868121

DATE FILED: September 24, 2001

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	11/007446	January 14, 1999

PCT-DATA:
APPL-NO: PCT/US00/00024
DATE-FILED: January 3, 2000
PUB-NO: WO00/42825
PUB-DATE: Jul 20, 2000
371-DATE:
102(E)-DATE:

US-CL-CURRENT: 428/690, 252/301.36 , 313/502 , 313/506 , 313/509 , 428/917

ABSTRACT:

The present invention provides an electroluminescent device comprising a transparent conductive layer, a binder layer placed on the back surface of the transparent conductive layer, a luminescent-particle layer comprising a substantially single layer of particles containing luminescent particles, which layer is applied on the back surface of the transparent conductive layer through the binder layer, an insulating layer comprising insulating particles, which is placed on the back surface of the luminescent-particle layer, and a rear electrode placed on the back surface of the insulating layer, in which the luminescent particles are embedded in the binder layer, or the luminescent particles are substantially not embedded in the insulating layer.

23 Claims, 1 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 1

---------- KWIC ---------

Detailed Description Text - DETX (22):
A dielectric constant may be decreased by the addition of glass bubbles

(glass balloons or hollow particles) to the layer of a binder layer on the insulating layer side to fill minute bubbles. In this case, the diameter of a bubble is preferably smaller than the particle size of luminescent particles, and is usually 10 .mu.m or less.

US-PAT-NO: 6565199

DOCUMENT-IDENTIFIER: US 6565199 B2
See image for Certificate of Correction

TITLE: Ink jet recording apparatus using recording unit with ink cartridge having ink inducing element

DATE-ISSUED: May 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ujita; Toshihiko	Kanagawa	N/A	N/A	JP
Takenouchi; Masanori	Kanagawa	N/A	N/A	JP
Tsukuda; Keiichiro	Kanagawa	N/A	N/A	JP

APPL-NO: 10/ 128389

DATE FILED: April 24, 2002

PARENT-CASE:

This application is a division of application Ser. No. 09/016,322, filed Jan. 30, 1998, now U.S. Pat. No. 6,454,399, which is a division of application Ser. No. 08/669,644, filed Jun. 24, 1996, now U.S. Pat. No. 5,784,088, which is a continuation of application Ser. No. 08/165,843, filed Dec. 14, 1993, now abandoned.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	5-179195	July 20, 1993
JP	5-298370	November 29, 1993
JP	5-298500	November 29, 1993
JP	5-298501	November 29, 1993

US-CL-CURRENT: 347/86

ABSTRACT:

An ink cartridge (3) including an ink reservoir portion having a porous member (37) for storing ink and an ink supply portion (39) has an ink inducing element (47) disposed between the ink reservoir portion and the ink supply portion (39). The ink inducing element (47) is made of bundle of fibers in which each fiber is disposed in parallel to the direction of ink supplying from the ink reservoir to the ink supply portion (39), and one end of the ink inducing element (47) is press-touched to the porous member (37).

19 Claims, 67 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 28

---------- KWIC ---------

Detailed Description Text - DETX (93):

However, occasionally a size of the air bubbles become glowing within the period described above under a bad environmental condition such as under both an extremely high temperature and a low relative humidity, and these grown air bubbles interrupt the ink flow to the recording head to cause its poor printing abilities. Especially in case of that the valve mechanism 614 is driven at the time of connecting or separating the ink-jet recording head 602 and the ink cartridge 601 as shown in FIG. 8A, the air from the outside may be introduced into a certain region of the ink path, which corresponds to an extent of the valve movement or the like. Therefore, the valve mechanism makes an unfavorable condition under the environment described above.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	23151	biolumines$ or fluorescen$ near4 protein$1 or luciferase$1 or photoprotein$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:40
L2	152305	bubble$	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:41
L3	24	1 same 2	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:42
L4	83381	toy or novelty	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:43
L5	46	1 and 2 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L6	28	1 same 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L7	40	1 and toy	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:45
L9	27	7 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L10	34	1 and novelty adj item$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 12:00
L11	18	10 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L12	286	((chemilumines$ or lumines$8 or glow$8) same 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:28
L13	29	((chemilumines$ or lumines$8 or glow$8) near4 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:32
L14	9	12 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:32

PGPUB-DOCUMENT-NUMBER: 20030090893

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030090893 A1

TITLE: Lighting system and device

PUBLICATION-DATE: May 15, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Nepil, James	Garfield	NJ	US	

APPL-NO: 10/ 005761

DATE FILED: November 12, 2001

US-CL-CURRENT: 362/101, 362/235 , 362/318 , 362/800 , 362/96

ABSTRACT:

The present invention is a light-producing technology exemplified by lighting that is safe, reliable, energy efficient, long lasting, and capable of operating under a wide range of weather and other conditions. The device incorporates a durable housing, a light element, a liquid solution, and a power supply. Subject only to its power source, it is capable of indefinitely producing intensely visible light at 100 yards or more during both daytime and nighttime. It can be configured for higher or lower intensities in a wide variety of foreseen applications. The device is not flammable, explosive, or toxic, and without loss of function withstands shock, extended water immersion, and heating and cooling to temperatures below freezing and approaching boiling.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (9):

[0007] The device of U.S. Pat. No. 4,967,321 to Cimock is a flashlight wand designed as a children's toy. The wand contains two DC batteries, a small incandescent bulb, and light reflecting objects. Light production of the Cimock device is limited. U.S. Pat. No. 5,392,203 to Harris, Jr. discloses a waterproof taxi light to guide aircraft on a tarmac. The device includes a lighted signal member with an elongate, translucent tubular member adapted for providing both daytime and nighttime illumination. The light source is a DC battery powered flashlight bulb. The translucent tube provides for light dispersion. Harris, Jr. discloses the use of a clear fluid within the translucent tubular member (column 6, lines 10-15), but the light element, a bulb, is not even partially submerged in the fluid. Thus, the light is not as intense as it could be if the light element were at least partially submerged in the fluid.

Summary of Invention Paragraph - BSTX (11):

[0009] U.S. Pat. No. 4,070,777 to Lo Giudice discloses a novelty display device incapable of producing intensely visible light. Designed for amusement, this device uses miniature lamps strung through the length of a liquid-filled housing to illuminate a continuous flow of bubbles through a liquid contained within a hollow glass tube. Boiling liquid heated by lighted bulbs is the

bubble source. The device is not only an inadequate means of producing high intensity lighting, but it is also not durable because the glass housing will likely shatter if dropped. U.S. Pat. No. 4,271,458 to George, Jr. discloses decorative light tubing for lighted tube displays. The device comprises a flexible tube containing a dielectric fluid (such as mineral oil or glycerin) and low voltage filament bulbs. However, this device is incapable of producing high-intensity lighting.

Summary of Invention Paragraph - BSTX (12):

[0010] U.S. Pat. No. 4,600,974 to Lew et al. discloses an optically decorated light baton with multiple purposes similar to the present prototype. It is a portable light tube with reflective platelets suspended in a medium, and in one embodiment phosphorescent or fluorescent material coats the light-emitting tube. The device of U.S. Pat. No. 5,165,781 to Orak is a novelty flashlight with color producing chambers intended for use as a toy or amusement. It comprises a low heat generating filament bulb and colored-fluid-containing transparent cups mounted to a power receiving housing. The light is not intensely visible because the bulb is at one end of the housing, which itself lacks fluid. The device requires continuous agitation to swirl the liquid colors. Although the housings of these two devices are fluid-filled, the light is not intensely visible partly because the light sources are located at only one end of the device where there is no fluid. Furthermore, although both devices utilize fluid mediums, both require agitation to obtain the full effect of the fluid: the Orak device requires agitation to swirl the liquid colors and the Lew et al. device requires agitation to make the light reflecting particles move through the fluid.

Summary of Invention Paragraph - BSTX (13):

[0011] U.S. Pat. No. 5,662,406 to Mattice discloses a lighted baby bottle designed for easy location in the dark. A filament bulb produces a low intensity glowing light and some heat. U.S. Pat. No. 5,993,021 to Lin discloses a decorative lamp designed for aquarium accent lighting. A tube containing water and artificial fish is illuminated by a low-intensity, heat-producing filament bulb not immersed in the fluid. A bubble valve produces air bubbles which cause the artificial fish to move.

US-PAT-NO: 6620017

DOCUMENT-IDENTIFIER: US 6620017 B1

TITLE: Bubble wand with ornaments within a container

DATE-ISSUED: September 16, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bitton; Mary Kay	Oak Park	CA	91377	N/A

APPL-NO: 10/ 128889

DATE FILED: April 23, 2002

US-CL-CURRENT: 446/16, 446/15 , 446/18

ABSTRACT:

A bubble wand with an ornamental figure and an ornamental bubble loop. The ornamental figure and ornamental loop are provided in the form of beads, shapes, letters, a small figurine of an animal, plant, person, cartoon character, action figure, or other attractive representation. The ornamental figure and loop are attached to the wand or are provided with a means for releasably or slidably attaching the ornamental figure to the wand or to a suction tube used in many soap dispensers.

10 Claims, 4 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 4

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Brief Summary Text - BSTX (6):

The devices and methods described below provide for mounting three-dimensional or two-dimensional art onto a bubble wand that is within a transparent container. The ornamental figure attached to the bubble wand can be used to provide amusement to children, as a means to make finding lost bubble wands easier, as a method of inducing children to bathe longer, as an inducement for both children and adults to use more soap or more bubble mixture, as an advertising medium and tie-in for commercial exploitation of characters, as a promotional item for various events, or merely as a novelty item. Note that the terms figure, figurine, ornamental figure, and ornamental figurine are used interchangeably herein.

Detailed Description Text - DETX (8):

As with the embodiment in FIG. 1, the bubble loop 5 and ornamental figure 4 may comprise any ornamental shape, including two- or three-dimensional shapes, animals, plants, things, characters, geometric patterns, and other ornamental designs. Moreover, the materials of the wand assembly, pump, dispensing tip, cap, or bottle may be made from a material that glows in the dark.

Detailed Description Text - DETX (10):
The various embodiments of the bubble wand with ornaments within a container may be packaged and marked to indicate their use as a bubble-making toy. Where the bubble mixture is soap, the embodiments should be packaged and marked to indicate its dual use as a bubble-making toy and as soap. The packages are displayed or placed so that prospective purchasers will find them with other bubble-making toys and with other soaps. Alternatively, the packages are placed by themselves or near unrelated products in order to generate more interest in the product. In addition, retailers may place associated displays, indicating the intended use of the various embodiments in proximity to the product, or elsewhere as a promotional display.

Claims Text - CLTX (1):
1. A toy suitable for making bubbles comprising: a container having an opening; a container cap releasably attached to the opening of the container; a bubble wand, having a shaft connected to a bubble loop, wherein the bubble wand is disposed within the container and wherein the bubble wand is releasably attached to the container cap; and an ornamental figure releasably attached to the bubble wand.

Claims Text - CLTX (2):
2. The toy of claim 1 wherein the bubble loop has an ornamental shape.

Claims Text - CLTX (3):
3. The toy of claim 1 wherein the shaft has an ornamental shape.

Claims Text - CLTX (4):
4. The toy of claim 1 wherein the container cap is a cap.

Claims Text - CLTX (5):
5. The toy of claim 1 wherein the container cap is a screw-on lid.

Claims Text - CLTX (6):
6. The toy of claim 1 wherein the container cap is a flip-top lid.

Claims Text - CLTX (7):
7. The toy of claim 1 wherein the container cap is a snap-top lid.

Claims Text - CLTX (8):
8. The toy of claim 1 wherein the container cap is a dispensing tip.

Claims Text - CLTX (9):
9. The toy of claim 1 wherein the container is filled with a bubble mixture.

Claims Text - CLTX (10):
10. The toy of claim 1 wherein the container is filled with a liquid soap suitable for producing bubbles.

US-PAT-NO: 6612712

DOCUMENT-IDENTIFIER: US 6612712 B2

TITLE: Lighting system and device

DATE-ISSUED: September 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Nepil; James	Garfield	NJ	07026	N/A

APPL-NO: 10/ 005761

DATE FILED: November 12, 2001

US-CL-CURRENT: 362/101, 362/318 , 362/806 , 362/96

ABSTRACT:

The present invention is a light-producing technology exemplified by lighting that is safe, reliable, energy efficient, long lasting, and capable of operating under a wide range of weather and other conditions. The device incorporates a durable housing, a light element, a liquid solution, and a power supply. Subject only to its power source, it is capable of indefinitely producing intensely visible light at 100 yards or more during both daytime and nighttime. It can be configured for higher or lower intensities in a wide variety of foreseen applications. The device is not flammable, explosive, or toxic, and without loss of function withstands shock, extended water immersion, and heating and cooling to temperatures below freezing and approaching boiling.

20 Claims, 3 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 1

---------- KWIC ---------

Brief Summary Text - BSTX (9):

The device of U.S. Pat. No. 4,967,321 to Cimock is a flashlight wand designed as a children's toy. The wand contains two DC batteries, a small incandescent bulb, and light reflecting objects. Light production of the Cimock device is limited. U.S. Pat. No. 5,392,203 to Harris, Jr. discloses a waterproof taxi light to guide aircraft on a tarmac. The device includes a lighted signal member with an elongate, translucent tubular member adapted for providing both daytime and nighttime illumination. The light source is a DC battery powered flashlight bulb. The translucent tube provides for light dispersion. Harris, Jr. discloses the use of a clear fluid within the translucent tubular member (column 6, lines 10-15), but the light element, a bulb, is not even partially submerged in the fluid. Thus, the light is not as intense as it could be if the light element were at least partially submerged in the fluid.

Brief Summary Text - BSTX (11):

U.S. Pat. No. 4,070,777 to Lo Giudice discloses a novelty display device incapable of producing intensely visible light. Designed for amusement, this device uses miniature lamps strung through the length of a liquid-filled housing to illuminate a continuous flow of bubbles through a liquid contained within a hollow glass tube. Boiling liquid heated by lighted bulbs is the bubble source. The device is not only an inadequate means of producing high intensity lighting, but it is also not durable because the glass housing will likely shatter if dropped. U.S. Pat. No. 4,271,458 to George, Jr. discloses decorative light tubing for lighted tube displays. The device comprises a flexible tube containing a dielectric fluid (such as mineral oil or glycerin) and low voltage filament bulbs. However, this device is incapable of producing high-intensity lighting.

Brief Summary Text - BSTX (12):

U.S. Pat. No. 4,600,974 to Lew et al. discloses an optically decorated light baton with multiple purposes similar to the present prototype. It is a portable light tube with reflective platelets suspended in a medium, and in one embodiment phosphorescent or fluorescent material coats the light-emitting tube. The device of U.S. Pat. No. 5,165,781 to Orak is a novelty flashlight with color producing chambers intended for use as a toy or amusement. It comprises a low heat generating filament bulb and colored-fluid-containing transparent cups mounted to a power receiving housing. The light is not intensely visible because the bulb is at one end of the housing, which itself lacks fluid. The device requires continuous agitation to swirl the liquid colors. Although the housings of these two devices are fluid-filled, the light is not intensely visible partly because the light sources are located at only one end of the device where there is no fluid. Furthermore, although both devices utilize fluid mediums, both require agitation to obtain the full effect of the fluid: the Orak device requires agitation to swirl the liquid colors and the Lew et al. device requires agitation to make the light reflecting particles move through the fluid.

Brief Summary Text - BSTX (13):

U.S. Pat. No. 5,662,406 to Mattice discloses a lighted baby bottle designed for easy location in the dark. A filament bulb produces a low intensity glowing light and some heat. U.S. Pat. No. 5,993,021 to Lin discloses a decorative lamp designed for aquarium accent lighting. A tube containing water and artificial fish is illuminated by a low-intensity, heat-producing filament bulb not immersed in the fluid. A bubble valve produces air bubbles which cause the artificial fish to move.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	23151	biolumines$ or fluorescen$ near4 protein$1 or luciferase$1 or photoprotein$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:40
L2	152305	bubble$	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:41
L3	24	1 same 2	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:35
L4	83381	toy or novelty	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:43
L5	46	1 and 2 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L6	28	1 same 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L7	40	1 and toy	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:45
L9	27	7 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L10	34	1 and novelty adj item$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 12:00
L11	18	10 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L12	286	((chemilumines$ or lumines$8 or glow$8) same 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:28
L13	29	((chemilumines$ or lumines$8 or glow$8) near4 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:32
L14	9	12 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:34
L15	0	12 and 2 adj bath	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:34
L16	145975	fluorescen$	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:35
L17	698	16 same 2	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:36
L18	12	17 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:49

PGPUB-DOCUMENT-NUMBER: 20040018974

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040018974 A1

TITLE: Multivalent constructs for therapeutic and diagnostic applications

PUBLICATION-DATE: January 29, 2004

US-CL-CURRENT: 514/12, 530/350

APPL-NO: 10/ 379287

DATE FILED: March 3, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60440201 20030115 US

non-provisional-of-provisional 60360821 20020301 US

RELATED APPLICATIONS

[0001] This application claims priority from U.S. Provisional Application Serial No. 60/440,201 filed on Jan. 15, 2003, and U.S. Provisional Application Serial No. 60/360,821, filed on Mar. 1, 2002, both of which are incorporated by reference

PGPUB-DOCUMENT-NUMBER: 20030092098

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030092098 A1

TITLE: Renilla reniformis fluorescent proteins, nucleic acids encoding the fluorescent proteins and the use thereof in diagnostics, high throughput screening and novelty items

PUBLICATION-DATE: May 15, 2003

US-CL-CURRENT: 435/69.1, 530/350

APPL-NO: 09/ 808898

DATE FILED: March 15, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60189691 20000315 US

RELATED APPLICATIONS

[0001] Benefit of priority under 35 U.S.C. .sctn.119(e) is claimed to U.S. provisional application Serial No. 60/189,691, filed Mar. 15, 2000, to Bryan et al., entitled "RENILLA RENIFORMIS FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS" is claimed.

[0002] This application is related to allowed U.S. application Ser. No. 09/277,716, filed Mar. 26, 1999, to Bruce Bryan and Christopher Szent-Gyorgyi, entitled "LUCIFERASES, FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE LUCIFERASES AND FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS." This application is related to International PCT application No. WO 99/49019 to Bruce Bryan and Prolume, LTD., entitled "LUCIFERASES, FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE LUCIFERASES AND FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS."

[0003] This application is also related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS", now U.S. Pat. No. 5,876,995, issued Mar. 2, 1999, and in U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASTIC TISSUE AND OTHER TISSUES". The application is also related to U.S. application Ser. No. 08/990,103, filed Dec. 12, 1997, to Bruce Bryan entitled "APPARATUS AND METHODS FOR DETECTING AND IDENTIFYING INFECTIOUS AGENTS".

PGPUB-DOCUMENT-NUMBER: 20030066096

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030066096 A1

TITLE: Bioluminescent novelty items

PUBLICATION-DATE: April 3, 2003

US-CL-CURRENT: 800/8, 162/162 , 42/54 , 424/450 , 424/456 , 424/70.14 , 442/131

APPL-NO: 09/ 729133

DATE FILED: December 1, 2000

RELATED-US-APPL-DATA:

child 09729133 A1 20001201

parent continuation-of 09444762 19991122 US PENDING

child 09729133 A1 20001201

parent continuation-of 09135988 19980817 US PATENTED

child 09729133 A1 20001201

parent continuation-in-part-of 08757046 19961125 US PATENTED

child 09729133 A1 20001201

parent continuation-in-part-of 08597274 19960206 US PATENTED

non-provisional-of-provisional 60079624 19980327 US

non-provisional-of-provisional 60089367 19980615 US

RELATED APPLICATIONS

[0001] This applicaiton is a continuation of U.S. application Ser. No. 09/444,762 to Bruce Bryan, filed Nov. 22, 1999, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also continuation of U.S. application Ser. No. 09/135,988 to Bruce Bryan, filed Aug. 17, 1998, now U.S. Pat. No. 6,152,358, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also continuation-in-part of U.S. application Ser. No. 08/757,046 to Bruce Bryan, filed Nov. 25, 1996, now U.S. Pat. No. 5,876,995, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also a continuation-in-part of U.S. application Ser. No. 08/597,274, now allowed, to Bruce Bryan, filed Feb. 6, 1996, entitled "BIOLUMINESCENT NOVELTY ITEMS".

[0002] U.S. application Ser. No. 09/444,762 is a continuation of U.S. application Ser. No. 09/135,988, which is a continuation-in-part of U.S. application Ser. No. 08/757,046, which is a continuation-in-part of U.S. application Ser. No. 08/597,274. The subject matter of each of U.S. application Ser. Nos. 09/135,988, 08/597,274 and 08/757,046 is herein incorporated in its entirety by reference thereto. This application is also

related to provisional application serial numbers 60/079,624 and 60/089,367. The disclosures of each of the above noted patents, applications and provisional applications is incorporated herein by reference thereto.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	23151	biolumines$ or fluorescen$ near4 protein$1 or luciferase$1 or photoprotein$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:40
L2	152305	bubble$	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:41
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L4	83381	toy or novelty	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:43
L5	46	1 and 2 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L6	28	1 same 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
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L9	27	7 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L10	34	1 and novelty adj item$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:53
L11	18	10 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L12	286	((chemilumines$ or lumines$8 or glow$8) same 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:28
L13	29	((chemilumines$ or lumines$8 or glow$8) near4 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:32
L14	9	12 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:34
L15	0	12 and 2 adj bath	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:34
L16	145975	fluorescen$	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:35
L17	698	16 same 2	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:36
L18	12	17 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:49
L19	33788	(toy or novelty adj item$1)	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:55
L20	71	16 and 2 and 19	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:55

PGPUB-DOCUMENT-NUMBER: 20040018974

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040018974 A1

TITLE: Multivalent constructs for therapeutic and diagnostic applications

PUBLICATION-DATE: January 29, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Arbogast, Christophe	Viuz - En - Sallaz	NJ	FR	
Bussat, Philippe	Feigers	NJ	FR	
Fan, Hong	Plainsboro	NJ	US	
Linder, Karen E.	Kingston	NJ	US	
Marinelli, Edmund R.	Lawrenceville	NJ	US	
Nanjappan, Palaniappa	Dayton	NJ	US	
Nunn, Adrian	Lamberville	NJ	US	
Pillai, Radhakrishna	Cranbury	NJ	US	
Pochon, Sibylle	Troinex	NJ	CH	
Ramalingam, Kondareddiar	Dayton	NJ	US	
Shrivastava, Ajay	Plainsboro	NJ	US	
Song, Bo	Princeton	MA	US	
Swenson, Rolf E.	Princeton	MA	US	
Wronski, Mathew A. Von	Moorestown	MA	US	
Sato, Aaron	Somerville	US		
Walker, Sharon Michele	North Attleboro	US		
Dransfield, Daniel T.	Hanson	US		

APPL-NO: 10/ 379287

DATE FILED: March 3, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60440201 20030115 US

non-provisional-of-provisional 60360821 20020301 US

US-CL-CURRENT: 514/12, 530/350

ABSTRACT:

The invention provides compositions and methods for therapeutic and diagnostic applications.

RELATED APPLICATIONS

[0001] This application claims priority from U.S. Provisional Application Serial No. 60/440,201 filed on Jan. 15, 2003, and U.S. Provisional Application Serial No. 60/360,821, filed on Mar. 1, 2002, both of which are incorporated by reference

---------- KWIC ---------

Brief Description of Drawings Paragraph - DRTX (2):

[0061] FIG. 1 shows the binding of fluorescent beads to KDR-transfected and mock-transfected cells. Neutravidin-coated beads with the indicated biotinylated ligands attached were tested for binding to KDR-expressing and non-expressing 293H cells. Specific binding to KDR was detected for both P5 (with hydrophilic spacer) and P6. Further details are provided in Example 2.

Brief Description of Drawings Paragraph - DRTX (17):

[0076] FIG. 16 shows that D1 potently blocks the migration/invasion of endothelial cells induced by VEGF. Migrating cells were quantitated by fluorescence measurement after staining the migrated cells with a fluorescent dye.

Brief Description of Drawings Paragraph - DRTX (39):

[0098] FIG. 37 is a graph showing uptake and retention of bubble contrast in the tumor up to 30 minutes post injection for suspensions of phospholipid stabilized microbubbles conjugated to a heteromultimeric construct.

Detail Description Paragraph - DETX (9):

[0106] The term "binding polypeptide" as used herein refers to any polypeptide capable of forming a binding complex with another molecule. Also included within the definition of "binding polypeptides" are polypeptides that are modified or optimized as disclosed herein. Specific examples of such modifications are discussed in detail infra, but include substitution of amino acids for those in the parent polypeptide sequence to optimize properties, obliterate an enzyme cleavage site, etc.; C- or N-terminal amino acid substitutions or elongations, e.g., for the purpose of linking the binding polypeptide to a detectable imaging label or other substrate, examples of which include, e.g., addition of a polyhistidine "tail" to assist in purification; truncations; amide bond changes; translocations; retroinverso peptides; peptoids; retroinversopeptoids; the use of N-terminal or C-terminal modifications or linkers, such as polyglycine or polylysine segments; alterations to include functional groups, notably hydrazide (--NH--NH.sub.2) functionalities or the C-terminal linker -Gly-Gly-Gly-Lys, to assist in immobilization of binding peptides according to this invention on solid supports or for attachment of fluorescent dyes; modifications which effect pharmacokinetics; structural modifications to retain structural features; formation of salts to increase water solubility or ease of formulation, and the like. In addition to the detectable labels described further herein, the binding polypeptides may be linked or conjugated to a radiotherapeutic agent, a cytotoxic agent, a tumorcidal agent or enzyme, a liposome (e.g., loaded with a therapeutic agent, an ultrasound appropriate gas, or both). In addition, binding polypeptides of the invention may be bound or linked to a solid support, such as a well, plate, bead, tube, slide, filter, or dish. Moreover, dimers or multimers of one or more binding polypeptides may be formed. Such constructs may, for example, exhibit increased ability to bind to the target. All such modified polypeptides are also considered "binding polypeptides" so long as they retain the ability to bind the targets. "Homologues" of the binding polypeptides described herein may be produced using any of the modification or optimization techniques described herein or known to those skilled in the art. Such homologous polypeptides will be understood to fall within the scope of the present invention and the definition of "binding polypeptides" so long as the substitution, addition, or deletion of amino acids or other such modification does not eliminate its ability to bind to the target. The term "homologous," as used herein, refers to the degree of sequence similarity between two polymers (i.e., polypeptide molecules or

nucleic acid molecules). When the same nucleotide or amino acid residue or one with substantially similar properties (i.e. a conservative substitution) occupies a sequence position in the two polymers under comparison, then the polymers are homologous at that position. For example, if the amino acid residues at 60 of 100 amino acid positions in two polypeptide sequences match or are homologous then the two sequences are 60% homologous. The homology percentage figures referred to herein reflect the maximal homology possible between the two polymers, i.e., the percent homology when the two polymers are so aligned as to have the greatest number of matched (homologous) positions. Polypeptide homologues within the scope of the present invention will be at least 70% and preferably greater than 80% homologous to at least one of the binding sequences disclosed herein.

Detail Description Paragraph - DETX (36):

[0131] In the practice of one embodiment of the present invention, a determination of the affinity of the heteromultimer or a constituent binding moiety for the target relative to another protein or target is a useful measure, and is referred to as affinity for the target. Standard assays for quantitating binding and determining affinity include equilibrium dialysis, equilibrium binding, gel filtration, or the monitoring of numerous spectroscopic changes (such as a change in fluorescence polarization) that may result from the interaction of the binding moiety and its target. These techniques or modifications thereof measure the concentration of bound and free ligand as a function of ligand (or protein) concentration. The concentration of bound heteromultimer or polypeptide ([Bound]) is related to the concentration of free heteromultimer or polypeptide ([Free]) and the concentration of binding sites for the polypeptide, i.e., on KDR, VEGF/KDR complex, cMet, or the cMet/HGF complex (N), as described in the following equation:

Detail Description Paragraph - DETX (74):

[0158] Lanthionines are readily prepared using known methods. See, for example, Robey et al. (Robey, F. A. and Fields, R. L. Anal. Biochem. (1989) 177, 373-377) and Inman, et al. (Inman, J. K.; Highet, P. F.; Kolodny, N.; and Robey, F. A. Bioconjugate Chem. (1991) 2, 458-463; Ploinsky, A. Cooney, M. C. Toy-Palmer, A. Osapay, G. and Goodman, M. J. Med. Chem. (1992) 35, 4185-4194; Mayer, J. P.; Zhang, J.; and Liu, C. F. in: Tam, J. P. and Kaumaya, P. T. P. (eds), "Peptides, Frontiers of Peptide Science," Proceedings of the 15.sup.th American Peptide Symposium, June 14-19 Nashville, Tenn. Klumer Academic Pub. Boston. pp 291-292;. Wakao, Norihiro; Hino, Yoichi; Ishikawa, Ryuichi. Jpn. Kokai Tokkyo Koho (1995), 7 pp. JP 07300452 A2 19951114 Heisei; JP 95-49692 19950309; JP 94-41458 19940311 have published in this area. Preparation of peptides using Boc automated peptide synthesis followed by coupling the peptide terminus with bromoacetic acid gives bromoacetylated peptides in good yield. Cleavage and deprotection of the peptides is accomplished using HF/anisole. If the peptide contains a cysteine group its reactivity can be controlled with low pH. If the pH of the medium is raised to 6-7, then either polymerization or cyclization of the peptide takes place. Polymerization is favored at high (100 mg/mL) concentration, whereas cyclization is favored at lower concentrations (1 mg/mL), e.g., in Scheme 1 below, 6 cyclizes to 7. 9

Detail Description Paragraph - DETX (100):

[0180] Furthermore, linkers which are combinations of the molecules and/or moieties described above, can also be employed to confer special advantage to the properties of the peptide. Lipid molecules with linkers may be attached to allow formulation of ultrasound bubbles, liposomes or other aggregation based

constructs. Such constructs could be employed as agents for targeting and delivery of a diagnostic reporter, a therapeutic agent (e.g. a chemical "warhead" for therapy), or a combination of these.

Detail Description Paragraph - DETX (105):

[0185] For detection of the target in solution, a heteromultimer according to the invention can be detectably labeled, e.g., fluorescently labeled, enzymatically labeled, or labeled with a radionuclide or paramagnetic metal or attached to bubbles, then contacted with the solution, and thereafter formation of a complex between the heteromultimer and the target can be detected. As an example, a fluorescently labeled KDR or VEGF/KDR complex binding heteromultimeric construct may be used for in vitro KDR or VEGF/KDR complex detection assays, wherein the heteromultimeric construct is added to a solution to be tested for KDR or VEGF/KDR complex under conditions allowing binding to occur. The complex between the fluorescently labeled KDR or VEGF/KDR complex binding heteromultimer and KDR or VEGF/KDR complex target can be detected and quantified by measuring the increased fluorescence polarization arising from the KDR or VEGF/KDR complex-bound heteromultimer relative to that of the free heteromultimer. Heteromultimers comprising cMet binding moieties may be used similarly.

Detail Description Paragraph - DETX (106):

[0186] Alternatively, a sandwich-type "ELISA" assay may be used, wherein a heteromultimeric construct is immobilized on a solid support such as a plastic tube or well, then the solution suspected of containing the target is contacted with the immobilized heteromultimeric construct, non-binding materials are washed away, and complexed target is detected using a suitable detection reagent, such as a monoclonal antibody recognizing the target. The monoclonal antibody is detectable by conventional means known in the art, including being detectably labeled, e.g., radiolabeled, conjugated with an enzyme such as horseradish peroxidase and the like, or fluorescently labeled.

Detail Description Paragraph - DETX (154):

[0234] Unless it contains a hyperpolarized gas, known to require special storage conditions, the lyophilized residue may be stored and transported without need of temperature control of its environment and in particular it may be supplied to hospitals and physicians for on site formulation into a ready-to-use administrable suspension without requiring such users to have special storage facilities. Preferably in such a case it can be supplied in the form of a two-component kit, which can include two separate containers or a dual-chamber container. In the former case preferably the container is a conventional septum-sealed vial, wherein the vial containing the lyophilized residue of step b) is sealed with a septum through which the carrier liquid may be injected using an optionally prefilled syringe. In such a case the syringe used as the container of the second component is also used then for injecting the contrast agent. In the latter case, preferably the dual-chamber container is a dual-chamber syringe and once the lyophilizate has been reconstituted and then suitably mixed or gently shaken, the container can be used directly for injecting the contrast agent. In both cases means for directing or permitting application of sufficient bubble forming energy into the contents of the container are provided. However, as noted above, in the stabilised contrast agents according to the invention the size of the gas microbubbles is substantially independent of the amount of agitation energy applied to the reconstituted dried product. Accordingly, no more than gentle hand shaking is generally required to give reproducible products with consistent microbubble size.

Detail Description Paragraph - DETX (160):

[0240] In accordance with the present invention, a number of optical parameters may be employed to determine the location of a target, such as a KDR, VEGF/KDR complex, cMet or HGF/cMet complex, with in vivo light imaging after injection of the subject with an optically-labeled heteromultimeric construct. Optical parameters to be detected in the preparation of an image may include transmitted radiation, absorption, fluorescent or phosphorescent emission, light reflection, changes in absorbance amplitude or maxima, and elastically scattered radiation. For example, biological tissue is relatively translucent to light in the near infrared (NIR) wavelength range of 650-1000 nm. NIR radiation can penetrate tissue up to several centimeters, permitting the use of heteromultimeric contructs of the invention to image target-containing tissue in vivo. For example, heteromultimeric constructs comprised of KDR, VEGF/KDR complex, cMet, or HGF/cMet binding polypeptides may be used for optical imaging of KDR, VEGF/KDR complex, cMet, or HGF/cMet complex in vivo.

Detail Description Paragraph - DETX (161):

[0241] In another embodiment, the heteromultimeric constructs of the invention may be conjugated with photolabels, such as optical dyes, including organic chromophores or fluorophores, having extensive delocalized ring systems and having absorption or emission maxima in the range of 400-1500 nm. The compounds of the invention may alternatively be derivatized with a bioluminescent molecule. The preferred range of absorption maxima for photolabels is between 600 and 1000 nm to minimize interference with the signal from hemoglobin. Preferably, photoabsorption labels have large molar absorptivities, e.g. >10.sup.5 cm.sup.-1M.sup.-1, while fluorescent optical dyes will have high quantum yields. Examples of optical dyes include, but are not limited to those described in WO 98/18497, WO 98/18496, WO 98/18495, WO 98/18498, WO 98/53857, WO 96/17628, WO 97/18841, WO 96/23524, WO 98/47538, and references cited therein. For example, the photolabels may be covalently linked directly to heteromultimers of the invention, such as, for example, heteromultimers comprised of KDR or VEGF/KDR complex binding peptides or linked to such a heteromultimers via a linker, as described previously.

Detail Description Paragraph - DETX (183):

[0263] The heteromultimeric constructs of the present invention can be used to improve the activity and/or efficacy of therapeutic agents by, for example, improving their affinity for or residence time at the target. In this embodiment heteromultimers are conjugated with the therapeutic agent. Alternatively, as discussed above, a liposome or bubble containing a therapeutic agent may be conjugated to heteromultimers of the invention. The therapeutic agent may be a radiotherapeutic, discussed above, a drug, chemotherapeutic or tumorcidal agent, genetic material, or a gene delivery vehicle, etc. The heteromultimer portion of the conjugate causes the therapeutic to "home" to the sites of target expression/localization and to improve the affinity of the conjugate for these sites, so that the therapeutic activity of the conjugate is more localized and concentrated at the target sites. For example, in one embodiment heteromultimers including KDR or VEGF/KDR complex binding polypeptides, can be used to improve the activity of therapeutic agents (such as anti-angiogenic or tumorcidal agents) against undesired angiogenesis such as occurs in neoplastic tumors, by providing or improving their affinity for KDR or the VEGF/KDR complex and their residence time at a KDR or VEGF/KDR complex on endothelium undergoing angiogenesis. In this aspect of the invention, hybrid agents are provided by conjugating KDR or

VEGF/KDR complex binding heteromultimers with a therapeutic agent. Such heteromultimeric constructs will be useful in treating angiogenesis associated diseases, especially neoplastic tumor growth and metastasis, in mammals, including humans. The method of treatment comprises administering to a mammal in need thereof an effective amount of a heteromultimeric construct comprising KDR or VEGF/KDR complex binding polypeptides conjugated with a therapeutic agent. The invention also provides the use of such conjugates in the manufacture of a medicament for the treatment of angiogenesis associated diseases in mammals, including humans. Heteromultimeric constructs of the invention comprising cMet or HGF/cMet complex binding moieties may be used similarly to treat disease associated with hyperproliferation or angiogenesis.

Detail Description Paragraph - DETX (219):
[0298] Fluorescence Anisotropy Measurements and BiaCore Assays

Detail Description Paragraph - DETX (220):
[0299] Fluorescence anisotropy measurements were performed in 384-well microplates in a volume of 10 .mu.L in binding buffer (PBS, 0.01% Tween-20, pH 7.5) using a Tecan Polarion fluorescence polarization plate reader. In some cases, heparin (0.5 .mu.g/mL) or 10% human serum was added to the binding buffer. The concentration of fluorescein labeled peptide was held constant (20 nM) and the concentration of KDR-Fc (or similar target) was varied. Binding mixtures were equilibrated for 10 minutes in the microplate at 30.degree. C. before measurement. The observed change in anisotropy was fit to Equation (1) below via nonlinear regression to obtain the apparent K.sub.D. Equation (1) assumes that the synthetic peptide and HSA form a reversible complex in solution with 1:1 stoichiometry: 1 r obs = r free + (r bound - r free) (K D + KDR + P) - (K D + KDR + P) 2 - 4 KDR P 2 P , (1)

Detail Description Paragraph - DETX (273):
[0338] The following experiments were performed to assess the ability of KDR-binding peptides to bind to KDR-expressing cells. In this experiment, KDR-binding peptides P5-B and P5-XB and P6-B and P6-XB were conjugated to fluorescent beads and their ability to bind to KDR-expressing 293H cells was assessed. The experiments show that both peptide sequences can be used to bind particles such as beads to KDR-expressing sites. In general, the P6 peptides exhibited better binding to the KDR expressing cells than P5. However, the binding of both peptides improved with the addition of a spacer.

Detail Description Paragraph - DETX (276):
[0341] Preparation of Peptide-Conjugated Fluorescent Beads

Detail Description Paragraph - DETX (277):
[0342] 0.1 mL of a 0.2 mM stock solution of each biotinylated peptide (prepared as set forth above, in 50% DMSO) was incubated with 0.1 mL of Neutravidin-coated red fluorescent microspheres (2 micron diameter, custom-ordered from Molecular Probes) and 0.2 mL of 50 mM MES (Sigma M-8250) buffer, pH 6.0 for 1 hour at room temperature on a rotator. As a positive control, biotinylated anti-KDR antibody was incubated with the Neutravidin-coated beads as above, except that 0.03 mg of the biotinylated antibody preparation in PBS (Gibco 14190-136) was used instead of peptide solution. Beads can be stored at 4.degree. C. until needed for up to 1 week.

Detail Description Paragraph - DETX (282):
[0347] To calculate the number of beads bound per well, a standard curve with increasing numbers of the same fluorescent beads was included in each assay plate. The standard curve was used to calculate the number of beads bound per well based on the fluorescence intensity of each well.

Detail Description Paragraph - DETX (477):
[0527] Serum-starved HUVECs were placed, 100,000 cells per well, into the upper chambers of BD Matrigel-coated FluoroBlok 24-well insert plates (#354141). Basal medium, containing either nothing or different attractants such as VEGF (10 ng/mL) or serum (5% FBS) in the presence or absence of potential VEGF-blocking/inhibiting compounds, was added to the lower chamber of the wells. After 22 hours, quantitation of cell migration/invasion was achieved by post-labeling cells in the insert plates with a fluorescent dye and measuring the fluorescence of the invading/migrating cells in a fluorescent plate reader. The VEGF-induced migration was calculated by subtracting the migration that occurred when only basal medium was placed in the lower chamber of the wells.

Detail Description Paragraph - DETX (555):
[0599] Serum-starved HUVECs were placed, 100,000 cells per well, into the upper chambers of BD fibronectin-coated FluoroBlok 24-well insert plates. Basal medium, with or without VEGF (10 ng/mL) in the presence or absence of increasing concentrations of PG-1 or D1, was added to the lower chamber of the wells. After 22 hours, quantitation of cell migration/invasion was achieved by post-labeling cells in the insert plates with a fluorescent dye and measuring the fluorescence of the invading/migrating cells in a fluorescent plate reader. VEGF-stimulated migration was derived by subtracting the basal migration measured in the absence of VEGF.

Detail Description Paragraph - DETX (611):
[0651] In this assay, complexes of control peptide and the test peptides (P30-XB, P31-XB, P32-XB) with .sup.125I-streptavidin in the presence or absence of VEGF (prepared as above) were tested for their ability to bind 293H cells that were transiently-transfected with KDR. The complex of P30-XB with .sup.125I-streptavidin specifically bound to KDR-transfected 293H cells as compared to mock transfected cells in the presence of VEGF (FIG. 31A), but not when VEGF was omitted (FIG. 31B). P30-XB was also the best KDR/VEGF complex binder among the peptides tested using fluorescence polarization and SPR (BiaCore) assays. See Table 9, U.S. S. No. 60/360,851, U.S. S. No. 60/440,441, and copending U.S.S.N. _____ entitled "KDR and VEGF/KDR Binding Peptides and Their Use in Diagnosis and Therapy," filed on the same date as the instant application and incorporated by reference herein in its entirety. This example shows that peptide (P30-XB) can specifically bind to The KDR/VEGF complex present on the cell surface. Therefore, it may possibly be used in targeting the KDR/VEGF complex in vitro and in vivo for diagnostic or therapeutic purposes. Since the KDR/VEGF binding peptide only detects the functional and active KDR receptor and not all the KDR present on cell surface, it may be useful in detecting and/or treating active angiogenesis in tumors, metastasis, diabetic retinopathy, psoriasis, and arthropathies. Furthermore, these peptides, as well as other peptides which bind KDR/VEGF complex may advantageously be included in hetermultimers of the invention.

Detail Description Paragraph - DETX (615):
[0654] Serum-starved HUVECs were placed, 100,000 cells per well, into the

upper chambers of BD fibronectin-coated FluoroBlok 24-well insert plates. Basal medium, with or without VEGF (10 ng/mL) in the presence or absence of D24 or D26, was added to the lower chamber of the wells. After 22 hours, quantitation of cell migration/invasion was achieved by post-labeling cells in the insert plates with a fluorescent dye and measuring the fluorescence of the invading/migrating cells in a fluorescent plate reader. The VEGF-induced migration was calculated for each experimental condition by subtracting the amount of migration that occurred when only basal medium was added to the lower chamber of the wells.

Detail Description Paragraph - DETX (621):

[0659] Serum-starved HUVECs were placed, 100,000 cells per well, into the upper chambers of BD fibronectin-coated FluoroBlok 24-well insert plates. Basal medium, with or without VEGF (10 ng/mL) in the presence or absence of varying concentrations of D6, or varying concentrations of D6 in combination with a constant 100 nM TK-1 (synthesized as described in WO 01/91805 A2) was added to the lower chamber of the wells. After 22 hours, quantitation of cell migration/invasion was achieved by post-labeling cells in the insert plates with a fluorescent dye and measuring the fluorescence of the invading/migrating cells in a fluorescent plate reader. VEGF-induced migration was calculated for each experimental conditions by subtracting the amount of migration observed in the absence of VEGF.

Detail Description Paragraph - DETX (635):

[0671] Serum-starved HUVECs were placed, 100,000 cells per well, into the upper chambers of BD fibronectin-coated FluoroBlok 24-well insert plates. Basal medium, containing either nothing or VEGF in the presence or absence of increasing concentrations of homodimeric D8 or heterodimeric D17, was added to the lower chamber of the wells. After 22 hours, quantitation of cell migration/invasion was achieved by post-labeling cells in the insert plates with a fluorescent dye and measuring the fluorescence of the invading/migrating cells in a fluorescent plate reader.

Detail Description Paragraph - DETX (731):

[0760] D23 (a dimeric construct of P6- and P12-derived sequences) was conjugated with a preparation of microbubbles as above described, according to the following methodology. The thioacetylated peptide (200 .mu.g) was dissolved in 20 .mu.l DMSO and then diluted in 1 ml of Phosphate Buffer Saline (PBS). This solution was mixed to the N-MPB-functionalized microbubbles dispersed in 18 ml of PBS-EDTA 10 mM, pH 7.5 and 2 ml of deacetylation solution (50 mM sodium phosphate, 25 mM EDTA, 0.5 M hydroxylamine.HCl, pH 7.5) was added. The headspace was filled with C.sub.4F.sub.10/Air (50/50) and the mixture was incubated for 2.5 hours at room temperature under gentle agitation (rotating wheel), in the dark. Conjugated bubbles were washed by centrifugation. Similarly, the monomer peptides making up D23 were separately conjugated to two different microbubble preparations according to the methodology described above.

Detail Description Paragraph - DETX (738):

[0767] When the P-6 derived sequence and the P12-derived sequence are separately attached to phospholipid stabilized microbubbles as monomers the resulting preparations achieve binding of the bubbles to KDR transfected cells in vitro to a different extent (3.5% & 16.8%). When a preparation of phospholipid stabilized microbubbles resulting from the addition of equal quantities of each of these peptide monomers (but the same total peptide load)

is tested in the same system 12.9% binding is achieved. Binding is a little more than the average of the two but as it is achieved with two sequences that bind to different sites on the target will be more resistant to competition at one or other of the sites on the target. However, for D23, the dimer, binding is increased to 22.9% (with the same peptide load). These results indicate that hetromultimers of the invention permit increased binding and increased resistance to competition.

Detail Description Paragraph - DETX (747):

[0776] Tumor imaging was performed using an ultrasound imaging system ATL HDI 5000 apparatus equipped with a L7-4 linear probe. B-mode pulse inversion at low acoustic power (MI=0.05) was used to follow accumulation of peptide conjugated-microbubbles on the KDR receptor expressed on the endothelium of neovessels. For the control experiments, an intravenous bolus of unconjugated microbubbles or microbubbles conjugated to non-specific peptide was injected. The linear probe was fixed on the skin directly on line with the implanted tumors and accumulation of targeted bubbles was followed during thirty minutes.

Detail Description Paragraph - DETX (748):

[0777] A perfusion of SonoVue.RTM. was administrated before injecting the test bubble suspension. This allows to evaluate the vascularization status and the video intensity obtained after SonoVue.RTM. injection is taken as an internal reference.

Detail Description Paragraph - DETX (751):

[0780] FIG. 37 shows uptake and retention of bubble contrast in the tumor up to 30 minutes post injection for suspensions of phospholipid stabilized microbubbles conjugated to a heteromultimeric construct of the invention prepared as described above (D23). In contrast, the same bubbles showed only transient (no more than 10 minutes) visualization/bubble contrast in the AOI situated outside the tumor site.

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ABSTRACT:

Composite gel articles shaped in the form of a body shaped suit for diving made by injection molding, extruding, spinning, casting, or dippingl.

RELATED APPLICATIONS

[0001] This application is a continuation-in-part of the following applications: Ser. Nos. 10/896047 filed Jun. 30, 2001; 10/273828 filed Oct. 17, 2002; 10/334542 filed Dec. 31, 2002; 10/299073 filed Nov. 18, 2002; 10/199364 filed Jul. 20, 2002; 09/721213 filed Nov. 21, 2001; 10/199361 filed Jul. 20, 2002; 10/199362 filed Jul. 20, 2002; 10/199363 filed Jul. 20, 2002; 09/517230, filed Mar. 2, 2000; 09/412886, filed Oct. 5, 1999; 09/285809, filed Apr. 1, 1999; 09/274498, filed Mar. 23, 1999; 08/130545, filed Aug. 8, 1998; 08/984459, filed Dec. 3, 1997; 08/909487, filed Jul. 12, 1997; 08/863794, filed May 27, 1997; PCT/US97/17534, filed Sep. 30, 1997; U.S. Ser. No. 08/719817 filed Sep. 30, 1996; U.S. Ser. No. 08/665343 filed Jun. 17, 1996 which is a Continuation-in-part of U.S. Ser. No. 08/612586 filed Mar. 8, 1996 (now U.S. Pat. No. 6,552,109); PCT/US94/04278 filed Apr. 19, 1994 (published May 26, 1995 No. WO95/13851); PCT/US94/07314 filed Jun. 27, 1994 (published Jan. 4, 1996 No. WO 96/00118); Ser. Nos. 08/288690 filed Aug. 11, 1994; 08/581188 filed Dec. 29, 1995; 08/581191 filed Dec. 29, 1995; 08/581125 filed Dec. 29, 1995 now U.S. Pat. No. 5,962,527. In turn U.S. Ser. Nos. 581,188; 581,191; and 581,125 (now U.S. Pat. No. 5,962,572) are continuation-in-parts of the following applications: Ser. Nos. 288,690, filed Aug. 11, 1994, PCT/US94/07314 filed Jun. 27, 1994 (CIP of PCT/US 94/04278, filed Apr. 19, 1994). The subject matter contained in the related

applications and patents are specifically incorporated herein by reference.

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Detail Description Paragraph - DETX (27):

[0074] Connectors, such as luer lock connectors, friction fit connectors, or other types of connectors for blood tubing especially useful for dialysis including use in connecting blood sets, hemodialysis tube sets, bubble trap inlet and outlet tubing, closures, caps and the like can be contaminated easily. A not so general information is that medical works do not take the time to decontaminate or safe guard connectors. The connectors are plug in and unplugged when needed and almost no one see to the cleanliness of the connectors before plug the connectors together, there is just no time for it. The need to plug and unplug connectors in the health service environment is that the connectors come in two types: male and female use to make every connection and the male and female parts come separately because at the time of manufacture they are made separately. The invention gel of high rigidity made from gel compositions of 250 to 400 parts by weight of block copolymers are useful for making tubing and tubing connectors. Surprisingly, if a male mold is use to made the male connector part, the male connector part can be allowed to cool in the mold and the same mold holding the male connector part can than be injected with additional gel of suitable rigidity to form the opposite female part. When the mold containing the male and female connector parts are cooled sufficient, both male and female connectors are demoted at the same time and packaged without contamination. The connectors can be molded with the same gel material tubing or if molded separately, the connectors need not be taken apart until needed. The novelty is that when the invention gels are sufficiently cooled to above room temperature, a second and followed by a third and the like molten gel can be in contact with the cooled gel and when both have cooled sufficiently the two parts will come apart. They do not bond in any way. Therefore a gel article negative can receive molten gel utilizing the negative gel to form a positive. This reduces the cost of making two molds, a positive and a negative. Only one is necessary to make both parts.

Detail Description Paragraph - DETX (39):

[0086] The invention gels of the invention can be formed into gel strands, gel bands, gel tapes, gel sheets, and other articles of manufacture in combination with or without other substrates or materials such as natural or synthetic fibers, multifibers, fabrics, films and the like. Moreover, because of their improved tear resistance and resistance to fatigue, the invention gels exhibit versatility as balloons for medical uses, such as balloon for valvuloplasty of the mitral valve, gastrointestinal balloon dilator, esophageal balloon dilator, dilating balloon catheter use in coronary angiogram and the like. Since the invention gels are more tear resistant, they are especially useful for making condoms, toy balloons, and surgical and examination gloves. As toy balloons, the invention gels are safer because it will not rupture or explode when punctured as would latex balloons which often times cause injures or death to children by choking from pieces of latex rubber. The invention gels are advantageously useful for making gloves, thin gloves for surgery and examination and thicker gloves for vibration damping which prevents damage to blood capillaries in the fingers and hand caused by handling strong shock and vibrating equipment. Various other gel articles can be made from the advantageously tear resistant gels and gel s of the inventions include gel suction sockets, suspension belts.

Detail Description Paragraph - DETX (180):

[0224] As taught in my U.S. application Ser. No. 08/288,690 filed Aug. 11, 1994, now U.S. Pat. No. 5,633,286 and specifically incorporated herein, additives useful in the gel of the present invention include: tetrakis[methylene 3,-(3'5'-tertbutyl-4"-hydroxyphenyl)propionate] methane, octadecyl 3-(3",5"-di-tert-butyl-4"-hydroxyphenyl) propionate, distearyl-pentaerythritol-diproprionate, thiodiethylene bis-(3,5ter-butyl-4-hydroxy) hydrocinnamate, (1,3,5-trimethyl-2,4,6-tris[-3,5-di-tert-butylhydroxybenzyl]benzene), 4,4"-methylenebis(2,6-di-tert-butylphenol), stearic acid, oleic acid, stearamide, behenamide, oleamide, erucamide, N,N"-ethylenebisstearamide, N,N"-ethylenebisoleamide, sterryl erucamide, erucyl erucamide, oleyl palmitamide, stearyl stearamide, erucyl stearamide, calcium sterate, other metal sterates, waxes (e.g. polyethylene, polypropylene, microcrystalline, carnauba, paraffin, montan, candelilla, beeswax, ozokerite, ceresine, and the like). The gel can also contain metallic pigments (aluminum and brass flakes), TiO2, mica, fluorescent dyes and pigments, phosphorescent pigments, aluminatrihydrate, antimony oxide, iron oxides (Fe3O4, --Fe2O3, etc.), iron cobalt oxides, chromium dioxide, iron, barium ferrite, strontium ferrite and other magnetic particle materials, molybdenum, silicone fluids, lake pigments, aluminates, ceramic pigments, ironblues, ultramarines, phthalocynines, azo pigments, carbon blacks, silicon dioxide, silica, clay, feldspar, glass microspheres, barium ferrite, wollastonite and the like. The report of the committee on Magnetic Materials, Publication NMAB-426, National Academy Press (1985) is incorporated herein by reference.

Detail Description Paragraph - DETX (182):

[0226] The invention gels are prepared by blending together the components including other additatives as desired at about 23.degree. C. to about 100.degree. C. forming a paste like mixture and further heating said mixture uniformly to about 150.degree. C. to about 200.degree. C. until a homogeneous molten blend is obtained. Lower and higher temperatures can also be utilized depending on the viscosity of the oils and amounts of multiblock copolymers and polymer used. These components blend easily in the melt and a heated vessel equipped with a stirrer is all that is required. Small batches can be easily blended in a test tube using a glass stirring rod for mixing. While conventional large vessels with pressure and/or vacuum means can be utilized in forming large batches of the invention gels in amounts of about 40 lbs or less to 10,000 lbs or more. For example, in a large vessel, inert gases can be employed for removing the composition from a dosed vessel at the end of mixing and a partial vacuum can be applied to remove any entrapped bubbles. Stirring rates utilized for large batches can range from about less than 10 rpm to about 40 rpm or higher.

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non-provisional-of-provisional 60322765 20010917 US

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ABSTRACT:

Various exemplary implementations of light emitting diode (LED) based illumination products and methods are disclosed including, but not limited to, glow sticks, key chains, toys, balls, various game accessories, light bulbs, night lights, wall lights, wall switches, wall sockets, wall panels, modular lights, flexible lights, automotive lights, wearable accessories, light ropes, decorative lights such as icicles and icicle strings, light tubes, insect control lights and methods, and lighted air fresheners/scent dispensers. Any of the foregoing devices may be equipped with various types of user interfaces (both "local" and "remote") to control light generated from the device.

Additionally, devices may be controlled via light control information or programs stored in device memory and/or transmitted or downloaded to the devices (e.g., devices may be controlled individually or collectively in groups via a network, glow sticks or other products may be downloaded with programming information that is stored in memory, etc.). Devices also may include sensors so that the generated light may change in response to various operating and/or environmental conditions or a user input. Various optical processing devices which may be used with any of the devices (e.g., reflectors, diffusers, etc.) also are disclosed.

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] The present application claims the benefit under 35 U.S.C. .sctn.119(e) of the following U.S. Provisional Applications:

[0002] Ser. No. 60/322,765, filed Sep. 17, 2001, entitled "Light Emitting Diode Illumination Systems and Methods;"

[0003] Ser. No. 60/329,202, filed Oct. 12, 2001, entitled "Light Emitting Diode Illumination Systems and Methods;"

[0004] Ser. No. 60/341,476, filed Oct. 30, 2001, entitled "Systems and Methods for LED Lighting;"

[0005] Ser. No. 60/335,679, filed Oct. 23, 2001, entitled "Systems and Methods for Programmed LED Devices;"

[0006] Ser. No. 60/341,898, filed Dec. 19, 2001, entitled "Systems and Methods for LED Lighting;" and

[0007] Ser. No. 60/353,569, filed Feb. 1, 2002, entitled "LED Systems and Methods."

[0008] This application also claims the benefit under 35 U.S.C. .sctn.120 as a continuation-in-part (CIP) of U.S. Non-provisional application Ser. No. 09/971,367, filed Oct. 4, 2001, entitled "Multicolored LED Lighting Method and Apparatus," which is a continuation of U.S. Non-provisional application Ser. No. 09/669,121, filed Sep. 25, 2000, entitled "Multicolored LED Lighting Method and Apparatus,"which is a continuation of U.S. Ser. No. 09/425,770, filed Oct. 22, 1999, now U.S. Pat. No. 6,150,774, which is a continuation of U.S. Ser. No. 08/920,156, filed Aug. 26, 1997, now U.S. Pat. No. 6,016,038.

[0009] This application also claims the benefit under 35 U.S.C. .sctn.120 as a continuation-in-part (CIP) of the following U.S. Non-provisional applications:

[0010] Ser. No. 09/805,368, filed Mar. 13, 2001, entitled "Light-Emitting Diode Based Products;"

[0011] Ser. No. 09/805,590, filed Mar. 13, 2001, entitled "Light-Emitting Diode Based Products;"

[0012] Ser. No. 09/215,624, filed Dec. 17, 1998, entitled "Smart Light Bulb;"

[0013] Ser. No. 09/213,607, filed Dec. 17, 1998, entitled "Systems and Methods for Sensor-Responsive Illumination;"

[0014] Ser. No. 09/213,189, filed Dec. 17, 1998, entitled "Precision Illumination;"

[0015] Ser. No. 09/213,581, filed Dec. 17, 1998, entitled "Kinetic Illumination;"

[0016] Ser. No. 09/213,540, filed Dec. 17, 1998, entitled "Data Delivery Track;"

[0017] Ser. No. 09/333,739, filed Jun. 15, 1999, entitled "Diffuse Illumination Systems and Methods;" and

[0018] Ser. No. 09/815,418, filed Mar. 22, 2001, entitled "Lighting Entertainment System," which is a continuation of U.S. Ser. No. 09/213,548, filed Dec. 17, 1998, now U.S. Pat. No. 6,166,496.

[0019] This application also claims the benefit under 35 U.S.C. .sctn.120 of each of the following U.S. Provisional Applications, as at least one of the above-identified U.S. Non-provisional applications similarly is entitled to the benefit of at least one of the following Provisional Applications:

[0020] Ser. No. 60/071,281, filed Dec. 17, 1997, entitled "Digitally Controlled Light Emitting Diodes Systems and Methods;"

[0021] Ser. No. 60/068,792, filed Dec. 24, 1997, entitled "Multi-Color Intelligent Lighting;"

[0022] Ser. No. 60/078,861, filed Mar. 20, 1998, entitled "Digital Lighting Systems;"

[0023] Ser. No. 60/079,285, filed Mar. 25, 1998, entitled "System and Method for Controlled Illumination;"

[0024] Ser. No. 60/090,920, filed Jun. 26, 1998, entitled "Methods for Software Driven Generation of Multiple Simultaneous High Speed Pulse Width Modulated Signals;"

[0025] Ser. No. 60/199,333, filed Apr. 24, 2000, entitled "Autonomous Color Changing Accessory;" and

[0026] Ser. No. 60/211,417, filed Jun. 14, 2000, entitled LED-Based Consumer Products."

[0027] Each of the foregoing applications is hereby incorporated herein by reference.

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Summary of Invention Paragraph - BSTX (2):

[0028] Lighting elements are sometimes used to illuminate a system, such as a consumer product, wearable accessory, novelty item, or the like. Existing illuminated systems, however, are generally only capable of exhibiting fixed illumination with one or more light sources. An existing wearable accessory, for example, might utilize a single white-light bulb as an illumination source, with the white-light shining through a transparent colored material. Such accessories only exhibit an illumination of a single type (a function of the color of the transparent material) or at best, by varying the intensity of the bulb output, a single-colored illumination with some range of controllable brightness. Other existing systems, to provide a wider range of colored illumination, may utilize a combination of differently colored bulbs. Such accessories, however, remain limited to a small number of different colored

states, for example, three distinct illumination colors: red (red bulb illuminated); blue (blue bulb illuminated); and purple (both red and blue bulbs illuminated). The ability to blend colors to produce a wide range of differing tones of color is not present.

Summary of Invention Paragraph - BSTX (4):

[0030] For example, many toys, such as balls, may benefit from improved color illumination processing, and/or networking attributes. There are toy balls that have lighted parts or balls where the entire surface appears to glow; however there is no ball available that employs dynamic color changing effects. Moreover, there is no ball available that responds to data signals provided from a remote source. As another example, ornamental devices are often lit to provide enhanced decorative effects. U.S. Pat. Nos. 6,086,222 and 5,975,717, for example, disclose lighted ornamental icicles with cascading lighted effects. As a significant disadvantage, these systems apply complicated wiring harnesses to achieve dynamic lighting. Other examples of crude dynamic lighting may be found in consumer products ranging from consumer electronics to home illumination (such as night lights) to toys to clothing, and so on.

Detail Description Paragraph - DETX (5):

[0086] An LED system is one type of illumination source. As used herein "illumination source" should be understood to include all illumination sources, including LED systems, as well as incandescent sources, including filament lamps, pyro-luminescent sources, such as flames, candle-luminescent sources, such as gas mantles and carbon arch radiation sources, as well as photo-luminescent sources, including gaseous discharges, fluorescent sources, phosphorescence sources, lasers, electro-luminescent sources, such as electro-luminescent lamps, light emitting diodes, and cathode luminescent sources using electronic satiation, as well as miscellaneous luminescent sources including galvano-luminescent sources, crystallo-luminescent sources, kine-luminescent sources, thermo-luminescent sources, triboluminescent sources, sonoluminescent sources, and radioluminescent sources. Illumination sources may also include luminescent polymers capable of producing primary colors.

Detail Description Paragraph - DETX (40):

[0121] As will be appreciated from the foregoing examples, an LED system such as that described in reference to FIGS. 1 & 2A-2B may be adapted to a variety of lighting applications, either as a replacement for conventional light bulbs, including incandescent light bulbs, halogen light bulbs, tungsten light bulbs, fluorescent light bulbs, and so forth, or as an integrated lighting fixture such as a desk lamp, vase, night light, lantern, paper lantern, designer night light, strip light, cove light, MR light, wall light, screw based light, lava lamp, orb, desk lamp, decorative lamp, string light, or camp light. The system may have applications to architectural lighting, including kitchen lighting, bathroom lighting, bedroom lighting, entertainment center lighting, pool and spa lighting, outdoor walkway lighting, patio lighting, building lighting, facade lighting, fish tank lighting, or lighting in other areas where light may be employed for aesthetic effect. The system could be used outdoors in sprinklers, lawn markers, pool floats, stair markers, in-ground markers, or door bells, or more generally for general lighting, ornamental lighting, and accent lighting in indoor or outdoor venues. The systems may also be deployed where functional lighting is desired, as in brake lights, dashboard lights, or other automotive and vehicle applications.

Detail Description Paragraph - DETX (56):

[0137] A system such as that described in reference to FIG. 1 may be incorporated into a toy, such as a ball. Control circuitry, a power supply, and LEDs may be suspended or mounted inside the ball, with all or some of the ball exterior formed of a light-transmissive material that allows LED color-changing effects to be viewed. Separate portions of the exterior may be formed from different types of light-transmissive material, or may be illuminated by different groups of LEDs to provide the exterior of the ball to be illuminated in different manners over different regions of its exterior.

Detail Description Paragraph - DETX (60):

[0141] A method of playing a game could be defined where the play does not begin until the ball is lighted or lighted to a particular color. The lighting signal could be produced from outside of the playing area by communicating through the transceiver, and play could stop when the ball changes colors or is turned off through similar signals. When the ball passes through a goal the ball could change colors or flash or make other lighting effects. Many other games or effects during a game may be generated where the ball changes color when it moves too fast or it stops. Color-changing effects for play may respond to signals received by the transceiver, respond to switches and/or transducers in the ball, or some combination of these. The game hot potato could be played where the ball continually changes colors, uninterrupted or interrupted by external signals, and when it suddenly or gradually changes to red or some other predefined color you have to throw the ball to another person. The ball could have a detection device such that if the ball is not thrown within the predetermined period it initiates a lighting effect such as a strobe. A ball of the present invention may have various shapes, such as spherical, football-shaped, or shaped like any other game or toy ball.

Detail Description Paragraph - DETX (61):

[0142] As will be appreciated from the foregoing examples, an LED system such as that described in reference to FIGS. 1 & 2A-2B may be adapted to a variety of color-changing toys and games. For example, color-changing effects may be usefully incorporated into many games and toys, including a toy gun, a water gun, a toy car, a top, a gyroscope, a dart board, a bicycle, a bicycle wheel, a skateboard, a train set, an electric racing car track, a pool table, a board game, a hot potato game, a shooting light game, a wand, a toy sword, an action figure, a toy truck, a toy boat, sports apparel and equipment, a glow stick, a kaleidoscope, or magnets. Color-changing effects may also be usefully incorporated into branded toys such as a View Master, a Super Ball, a Lite Brite, a Harry is Potter wand, or a Tinkerbell wand.

Detail Description Paragraph - DETX (115):

[0196] In an embodiment, the optic may include imperfections, coatings or the like (collectively referred to herein as imperfections) that are not uniformly distributed along its length. For example, FIG. 45 illustrates an optic 4502 with a greater frequency of imperfections 4506 in the middle of the optic as compared to the ends of the optic. The imperfections 4506 may be in the bulk of the optic material 4502 or on or near the surface of the material 4502. In an embodiment, the imperfections 4506 may be marks, bubbles, or other imperfections in or on the material. In an embodiment, the imperfections may be uniformly distributed but they may not be of similar size. For example, the imperfections towards the ends of the optic may be smaller than the ones towards the middle of the optic. In an embodiment, the imperfections may be the result of a coating that is applied to the surface of the optic 4502. For example, 3M manufactures a material that includes imperfections and the size of

imperfections in the material increases further away from the ends. The material is referred to as Conformable Lighting Element.

Detail Description Paragraph - DETX (118):

[0199] The lighting device 4200 including an elongated optic as discussed above may have a number of applications. For example, the device may be used to provide illumination in any environment in which flourescent or other tubular shaped lighting elements formerly were used (e.g., various office, warehouse, and home spaces such as under cabinets in a kitchen). In this application, the devices 4200 may be aligned in much the same way as fluorescent systems are mounted. One strip of lighting may comprise a number of individual lighting devices 4200, for example, that may be controlled individually, collectively, or an any subset of groups, according to the various concepts discussed herein (e.g., a networked lighting system). In such a system, a central controller may be provided as a separate device or as an integral part of one of the lighting devices 4200, making a master/slave relationship amongst the group of lighting devices.

Detail Description Paragraph - DETX (141):

[0222] FIG. 54 illustrates another embodiment of the present invention. The diffusing surface 5302 in this embodiment includes imperfections 5402 in the bulk or on the surface of the material. The imperfections may be arranged such that they get larger and or more frequent with distance from the illumination device 500. This arrangement may be used to generate substantially uniform illumination from the lighting device 5000. The imperfections may be bubbles in the material, for example, or the imperfections may form a pattern on the surface of the material. A pattern on the surface of the material may include areas where not much light is able to pass through and other areas where the is light is allowed to pass with higher transmission. The relative ratio of transmitting area to non-transmitting area may change as a function of the distance from the illumination device 5000. For example, the transmitting area may increase as the distance from the LEDs increases. This arrangement may provide substantially uniform illumination from the lighting device 5000. The areas where light transmission is low may include areas of high reflectivity to maximize the overall lighting efficacy. Materials to obtain such lighting effects are available from 3M Corporation, for example, and are referred to as Conformable Lighting Element.

Detail Description Paragraph - DETX (145):

[0226] Conventional "bug lights" typically include yellow incandescent lights that do not repel bugs but simply attract them less, as compared to a normal white incandescent light bulb. Light traps, used widely in food processing applications, employ fluorescent-style UV sources to attract and then electrocute insects via charged plates or grids, and then collect the fried insect parts into a pan or other container.

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DOCUMENT-IDENTIFIER: US 20030130407 A1

TITLE: Tear resistant gelatinous elastomer compositions and articles for use as fishing bait

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INVENTOR-INFORMATION:

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parent-patent 5467626 US

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US-CL-CURRENT: 524/505

ABSTRACT:

A soft gelatinous elastomer composition and article useful as fishing bait formed from one or a mixture of two or more of a hydrogenated styrene isoprene/butadiene block copolymer(s) and one or more plasticizers being in sufficient amounts to achieve a gel rigidity of from about 20 gram Bloom to about 1,800 gram Bloo

RELATED APPLICATIONS

[0001] This application is a continuation-in-part of the following applications: Ser. Nos. 09/896,047 filed Jun. 30, 2001; 09/721,213 filed Nov. 21, 2001; 09/421,886, filed Oct. 5, 1999; 09/285,809 filed Apr. 1, 1999, which are continuation-in-pat of U.S. Ser. No. 09/274,498, filed Mar. 23, 1999; Ser. No. 08/130,545, filed Aug. 8, 1998; Ser. No. 08/984,459, filed Dec. 3, 1997; Ser. No. 08/909,487, filed Jul. 12, 1997 (now U.S. Pat. No. 6,050,871); Ser. No. 08/863,794, filed May 27, 1997 (now U.S. Pat. No. 6,117,176); PCT/US97/17534, filed Sep. 30, 1997; U.S. Ser. No.: 08/719,817 filed Sep. 30, 1996 (now U.S. Pat. No. 6,148,830), U.S. Ser. No.: 08/665,343 filed Jun. 17, 1996 which is a Continuation-in-part of U.S. Ser. No: 612,586 filed Mar. 8, 1996; PCT/US94/04278 filed Apr. 19, 1994 (published May 26, 1995 No. WO95/13851) (now U.S. Pat. No. 6,033,283); PCT/US94/07314 filed Jun. 27, 1994 (published Jan. 4, 1996 No. WO96/00118) (now U.S. Pat. No. 5,868,597); Ser. No. 288,690 filed Aug. 11, 1994 (now U.S. Pat. No. 5,633,266); Ser. No. 581,188 filed Dec. 29, 1995; Ser. No. 581,191 filed Dec. 29, 1995 (now U.S. Pat. No. 5,760,117); Ser. No. 581,125 filed Dec. 29, 1995 now U.S. Pat. No. 5,962,527. In turn U.S. Ser. Nos. 581,188; 581,191; and 581,125 are continuation-in-parts of the following applications: Ser. Nos.: 288,690; PCT/US94/07314 which is a CIP of PCT/US94/04278. This application (docket #46) is being filed even date with the following multiple applicaitons having titles: (1) "GELATINOUS ELASTOMER COMPOSITIONS AND ARTICLES FOR USE AS FISHING BAIT", Docket #45, (2) "TEAR RESISTANT GELATINOUS ELASTOMER COMPOSITIONS AND ARTICLES FOR USE AS FISHING BAIT", Docket #46, (3) "GELATINOUS FOOD-ELASTOMER COMPOSITIONS AND ARTICLES FOR USE AS FISHING BAIT", Docket #47, (4) "GELATINOUS FOOD-ELASTOMER COMPOSITIONS AND ARTICLES", docket #48. The subject matter contained in the related applications and patents are specifically incorporated herein by reference.

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Detail Description Paragraph - DETX (184):
[0197] If the amount of a gas in oil exceeds saturation, small **bubbles** will form, remain suspended, and the oil will appear hazy. This is called entrained gas. The **bubbles** slowly rise to the surface. **Bubbles** of a gas, such as air, in an oil film cause holes that reduce oil film continuity and decrease the film's ability to prevent solid-to-solid contact.

Detail Description Paragraph - DETX (185):
[0198] The relative tendency of various oils to release entrained gas is measured by a gas **bubble** separation method ASTM D 3427. The method uses a cylinder-like test vessel with gas inlet and outlet ports. Air, or another gas (if of interest), is introduced into the bottom of the vessel at a specified temperature and flow rate. At the end of seven minutes the gas flow is stopped and the change in density as measured by a densitometer is recorded. The test is complete when the total volume of entrained air is reduced to 0.20% by

volume. The results are reported as the time it took for the oil to attain this value.

Detail Description Paragraph - DETX (186):

[0199] Foaming is defined as the production and coalescence of gas bubbles on a lubricant surface. Foam may be a result of a variety of problems including air leaks, contamination, and over filling of sumps. Foaming can cause loss of oil out of a vent and serious operational problems in most lubricated systems. Excessive foam can starve bearings and pumps of liquid lubricant (pump cavitation) causing failure, and cause poor performance in hydraulic systems. The foaming characteristics of an oil are measured by ASTM D-892. Using a calibrated porous stone, air is blown into the bottom of a graduated cylinder for a specified time. Immediately upon completion of the blowing period, the foam that has formed on the top of the oil is measured. Ten minutes after the completion of the blowing period, an additional measurement is made of the remaining foam as the foam retention characteristics of the oil. The results are reported in milliliters.

Detail Description Paragraph - DETX (223):

[0236] The present invention gel can also contain useful amounts of conventionally employed additives such as stabilizers, antioxidants, antiblocking agents, colorants, fragrances, flame retardants, flavors, other polymers in minor amounts and the like to an extend not affecting or substantially decreasing the desired properties. Additives useful in the gel of the present invention include: tetrakis[methylene 3,-(3'5'-di-tertbutyl-4"-hydroxyphenyl) propionate]methane, octadecyl 3-(3",5"-di-tert-butyl-4"-hydroxyphenyl) propionate, distearyl-pentaerythritol-diproprionate, thiodiethylene bis-(3,5-ter-butyl-4-hydroxy) hydrocinnamate, (1,3,5-trimethyl-2,4,6-tris-[3,5-di-tert-butyl-4-hydroxybenzyl]benzene), 4,4"-methylenebis(2,6-di-tert--butylphenol), Tinuvin P, 123, 144, 213, 234, 326, 327, 328, 571, 622, 770, 765, Chimassorb 119, 944, 2020, Uvitex OB, Irganox 245, 1076, 1098, 1135, 5057, HP series: 2215, 2225, 2921, 2411, 136, stearic acid, oleic acid, stearamide, behenamide, oleamide, erucamide, N,N"-ethylenebisstearamnide, N,N"-ethylenebisoleamide, sterryl erucamide, erucyl erucamide, oleyl palmitamide, stearyl stearamide, erucyl stearamide, calcium sterate, other metal sterates, waxes (e.g. polyethylene, polypropylene, microcrystalline, carnauba, paraffin, montan, candelilla, beeswax, ozokerite, ceresine, and the like). The gel can also contain metallic pigments (aluminum and brass flakes), TiO2, mica, fluorescent dyes and pigments, phosphorescent pigments, aluminatrihydrate, antimony oxide, iron oxides (Fe3O4,--Fe2O3, etc.), iron cobalt oxides, chromium dioxide, iron, barium ferrite, strontium ferrite and other magnetic particle materials, molybdenum, silicone fluids, lake pigments, aluminates, ceramic pigments, ironblues, ultramarines, phthalocynines, azo pigments, carbon blacks, silicon dioxide, silica, clay, feldspar, glass, microspheres, barium ferrite, wollastonite and the like. The report of the committee on Magnetic Materials, Publication NMAB-426, National Academy Press (1985) is incorporated herein by reference.

Detail Description Paragraph - DETX (239):

[0252] The invention gels are prepared by blending together the components (I, II, or III) including the various additives as desired at about 23.degree. C. to about 100.degree. C. forming a paste like mixture and further heating said mixture uniformly to about 150.degree. C. to about 200.degree. C. until a homogeneous molten blend is obtained. Lower and higher temperatures can also be utilized depending on the viscosity of the oils and amounts of multiblock

copolymers (I) and polymer (III) used. These components blend easily in the melt and a heated vessel equipped with a stirrer is all that is required. Small batches can be easily blended in a test tube using a glass stirring rod for mixing. While conventional large vessels with pressure and/or vacuum means can be utilized in forming large batches of the instant compositions in amounts of about 40 lbs or less to 10,000 lbs or more. For example, in a large vessel, inert gases can be employed for removing the composition from a closed vessel at the end of mixing and a partial vacuum can be applied to remove any entrapped bubbles. Stirring rates utilized for large batches can range from about less than 10 rpm to about 40 rpm or higher.

Detail Description Paragraph - DETX (240):

[0253] The invention gel can also contain gases as an additive, i.e. the gel can be foamed. Foam is herein defined as tightly or loosely packing aggregation of gas bubbles, separated from each other by thin or thick layers of gel. Many types of foamed invention gels (from ultra high density to ultra low density) can be produced as desired by (i) adding gas to the molten gel during processing, and (ii) producing gas in the molten gel during processing. Gas can be added by whipping a gas into the molten gel before it cools or introduce a gas into the molten gel and then expand or reduce the size of the gas bubbles by reducing the pressure to reduce the bubbles size or applying high pressure to expand the bubbles size. In this regard, inert gases such as Carbon dioxide, Nitrogen, Helium, Neon, Argon, Krypton, Xenon and Radon are suitable. Air can also be used. Gas can be produced in the molten gel by adding one or more of a "blowing agent" to the. Useful blowing agents include dinitroso compounds, such as dinitroso pentamethylene-tetramine, azodicarbonamide, 4,4'oxybis (benzenesulfonyl) hydrazine, 5-phenyltetrazole, p-toluenesulfonyl semicarbazide, sulfonyl hydrazide, such as benzene sulfonylhydrazide. Water can be used as a "blowing agent" to .sup.1 produce varying density of foam invention gels; water used to advantage can be in the form of mist, droplets, steam, and hot or cold water. The density of the foam invention gels can vary from less than 1.00 kilograms per cubic meter to near the solid gel density. Although the materials forming soft solid invention gels may be more shear resistant, the same materials when made into a foam become much less shear resistant.

Detail Description Paragraph - DETX (244):

[0257] As the invention gels formed from multiblock copolymers (I) having more and more midblock polymer chains can be expected to exhibit greater delay recovery form extension or longer relaxation times with increasing number of midblocks and increasing midblock lengths, such invention gels having more than three midblocks forming the copolymers (I) can exhibit extreme tear resistance and excellent tensile strength while at the same time exhibit almost liquid like properties. For example, a fun toy can be made from (S-E-EB-E-S), (S-B-EB-EB-S), (S-E-EP-E-EP-S), (S-P-EB-P-EB-S), (S-E-EB-E-EB-E-S), (S-E-EP-E-EP-E-EP-E-S), (S-E-EP-EP).sub.n, (S-B-EP-E-EP).sub.n, (S-E-EP-E-EP-E).sub.n, (S-E-EB-E-EB-E-EB-E-EB-S).sub- .n copolymer invention gels which are molded into cube shapes when placed on the surface of a incline will collect it self together and flow down the incline as a moving body much like a volume of water moving on a high surface tension surface. This is due to the greater distance between the end block (A) domains. Such liquid like performing invention gels can be very strong and exhibit extreme tear resistance as exhibited by invention gels made from (S-E-EP-S) multiblock copolymer invention gels with shorter (A) distance between domains. Such liquid like invention gels when shaped into a cube will be deformed by the force of gravity on Earth, but will retain its memory and regain to its molded cube shape when released in outer space or reform into a cube if let loose in a

container of liquid of equal density. As a comparison, such a toy formed in the shape of a large cube from a high viscosity triblock copolymer with a plasticizer content of 1:1,600 parts will be flattened by the force of gravity and run down an incline, but is very fragile and will start to tear if attempt is made to pick it up by hand. This is an excellent comparison of the difference of tear resistance difference between triblock copolymer gels and multiblock copolymer invention gels. A useful application is to use such an elastic liquid gel volume to fill a container or to encapsulate an electrical or electronic component in a container filling every available space, when needed, the shapeless gel volume can be removed by pouring it out of the container whole.

Detail Description Paragraph - DETX (253):

[0266] The invention gel can be formed into gel strands, gel bands, gel tapes, gel sheets, and other articles of manufacture in combination with or without other substrates or materials such as natural or synthetic fibers, multifibers, fabrics, films and the like. Moreover, because of their improved tear resistance and resistance to fatigue, the invention gels exhibit versatility as balloons for medical uses, such as balloon for valvuloplasty of the mitral valve, gastrointestinal balloon dilator, esophageal balloon dilator, dilating balloon catheter use in coronary angiogram and the like. Since the invention gels are more tear resistant, they are especially useful for making condoms, toy balloons, and surgical and examination gloves. As toy balloons, the invention gels are safer because it will not rupture or explode when punctured as would latex balloons which often times cause injures or death to children by choking from pieces of latex rubber. The invention gels are advantageously useful for making gloves, thin gloves for surgery and examination and thicker gloves for vibration damping which prevents damage to blood capillaries in the fingers and hand caused by handling strong shock and vibrating equipment. Various other gel articles can be made from the advantageously tear resistant invention gels and invention gel composites of the inventions include gel suction sockets, suspension belts,

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TITLE: Oncofetal antigen specific T-lymphocyte mediated immune response: manipulation and uses of oncofetal antigen specific CD4, CD8 cytotoxic and suppressor T cells and interleukin-10

PUBLICATION-DATE: July 3, 2003

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ABSTRACT:

Disclosed are methods for detecting cancer or determining the success of cancer therapy in an individual. These methods are based on analyzing the presence or frequency of cloned oncofetal antigen (OFA)- or immature laminin receptor protein (iLRP)-specific T lymphocyte subclasses obtained from the individual and which are stimulated with 44 kD OFA or iLRPA. A frequency of CD8 cytotoxic T cells relative to CD8 T suppressor cells indicates effectiveness of therapy, and a likelihood that protective immunity will develop. Also disclosed are kits for conducting these methods. Further disclosed are methods of rendering T suppressor lymphocytes cytotoxic, and methods of clonally expanding cytotoxic T lymphocytes in vivo.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation U.S. application Ser. No. 09/173,912, filed Oct. 16, 1998, which is a continuation-in-part of U.S. application Ser. No. 08/835,069, filed Apr. 4, 1997, now U.S. Pat. No. 6,335,174, issued Jan. 1, 2002, and which claims priority to provisional

application U.S. Ser. No. 60/014,903, filed Apr. 5, 1996.

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Brief Description of Drawings Paragraph - DRTX (36):

[0052] FIG. 34. Expression of OFA by MCA1315 murine fibrosarcoma cells and its inhibition by iLRP. Surface expression of OFA on MCA1315 cells was determined by immunostaining with the OFA-specific mAb 69.1 and flow cytometry (left panel). Incubation of the mAb 69.1 with iLRP before immunostaining decreases the intensity of the fluorescence drastically (right panel). White: Cells stained with mAb 69.1. Black: Cells stained with an isotype control mAb (MOPC-104E). Results are expressed as log fluorescence intensity (at 488 nm) in arbitrary units versus relative cell numbers.

Detail Description Paragraph - DETX (31):

[0082] In addition, the presence of IL-10 or IL-10 mRNA in CD8+ T cells, which in preferred embodiments, is detected with two and three color fluorescence in fixed and permeabilized T-cell flow cytometry using either in peripheral blood lymphocytes or in tumor infiltrating lymphocytes in the tissues of the residual tumor bed, indicates a strong potential for tumor promotion and cancer regrowth. Thus, detecting IL 10 levels in culture supernatants of clonally expanded T-cells or in tumor infiltrating lymphocyte-containing biopsy tissues taken from the tumor bed provides yet another technique for distinguishing the various clones of T cell subclasses and monitoring the progression of disease or the effectiveness of therapy. A kit for this method of measuring IL-10 levels would also include an anti-IL-10 monoclonal antibody or probes specific for detecting IL-10 mRNA.

Detail Description Paragraph - DETX (61):

[0106] At the time of the two week restimulation of the clones to maintain their proliferation, the cloned cells were harvested, washed in IMDM, and a viability count was done. A portion of the cells was saved out to be used in the cytotoxicity assay. Into 8 wells of V-bottomed 96 well plates, were placed 200 .mu.l of medium-washed target 5T lymphoma cells such that there were 10,000 cells/well in the target spontaneous release control and the target maximal release control wells. Into 6 wells/clone of V-bottomed 96 well plates were placed 100 .mu.l of medium-washed target 5T lymphoma cells such that there were 10,000 live target cells/well. Into each of two wells/clone was added 100 .mu.l of medium-washed cloned T cells at 12.5 clone cells: 1 target cell, 25 clone cells: 1 target cells, or 50 clone cells: 1 target cell. These are the experimental wells. Into 6 wells/clone were placed 200 .mu.l of medium-washed cloned T cells at the same concentrations as in the experimental wells except that no target cells are present. These served as the effector spontaneous release wells. The 96 well plates were centrifuged at 250.times.g for 4 minutes to pellet all cells and then incubated for 4 hours at 37.degree. C. in a humidified, 95% air/5% CO.sub.2 atmosphere. At the end of this incubation, 10 .mu.l of 10.times.lysis solution/100 .mu.l of medium was added to each of the maximal release wells to lyse the targets. The plates were then continued to be incubated at 37.degree. C. for another 45 minutes. The plates were then centrifuged at 250.times.g for 4 minutes to pellet remaining cells and 50 .mu.l of culture supernatant from all wells was transferred to a flat-bottomed 96 well ELISA plate. 50 .mu.l of reconstituted substrate mix in assay buffer was then added to each well and the plates were incubated at room temperature for 30 minutes. This substrate solution contained lactate, NAD (nicotinamide-adenine dinucleotide), INT (p-idonitrotetrazolium violet chloride), tetrazolium salt, and the enzyme diaphorase at optimal

concentrations for these volumes. 50 .mu.l of stop solution was added to each well, any bubbles were removed and the absorbance at 492 nm wavelength was determined using a Biotek ELISA reader.

Detail Description Paragraph - DETX (164):

[0188] n. While it has been shown that the amount of fluorescence detected for most intracellular cytokines is proportional to the amount found secreted by those same cells in culture supernatants, [Elson, et al., J. Immunol. 154:4294 (1995); Jung, et al., J. Immunol. Methods 159:197 (1993)] that is not the case for interferon. Elson, et al., supra.; Vikingson, et al., J. Immunol. Methods 173:219 (1994). Thus, culture supernatants are taken 48 hours and 96 hours after restimulation of clones and of uncloned, tumor-reactive cancer patient peripheral blood T cells and assay by ELISA for interferon--as described previously. Rohrer, J. W. et al., supra.

Detail Description Paragraph - DETX (267):

[0289] 51. Rosenberg, S. A., B. S. Packard, P. M. Aebersold, D. Solomon, S. L. Topalian, S. T. Toy, P. Simon, M. T. Lotze, J. C. Yang, C. A. Seipp, C. Simpson, C. Carter, S. Bock, D. Schwartzentruber, J. P. Wei, and D. E. White. 1988. Use of tumor infiltrating lymphocytes and interleukin-2 in the immunotherapy of patients with metastatic melanoma: Preliminary report. N. Eng. J. Med. 319:1676.

Detail Description Paragraph - DETX (423):

[0442] MCA-1315 cells grown in culture were harvested by treatment with PBS-EDTA, washed in staining buffer (PBS; pH 7.4, 2% BSA, and 0.1 sodium azide) and aliquoted at 2.5.times.10.sup.4 cells/sample. Cells were incubated with the appropriate dilution of anti-OFA mAb in staining buffer, either alone or with 1-5 .mu.g of iLRP for 1 h at 4.degree. C. An aliquot of cells was also stained with control mouse IgM (MOPC-104E) at the same dilution (10 .mu.g/ml). The excess primary Ab was removed by washing, and FITC-labeled goat antimouse IgM (Organon Teknika Corp., West Chester, Pa.) was added for 30 min at 4.degree. C. as second reagent for indirect immunofluorescent staining. Flow cytometry was performed using a FACS 440 (Becton Dickinson, San Jose, Calif.) equipped with WinMDI software. Flow cytometry data are depicted as histograms of cell number (y-axis) vs. fluorescence intensity (x-axis) on a log scale from representative experiments.

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TITLE: Microfabricated lenses, methods of manufacture thereof, and applications therefor

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ABSTRACT:

Microfabricated lenses, e.g., solid immersion lens (SIL) structures, are provided along with techniques for constructing these lens structures, as well as selected applications of such lens structures.

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit of U.S. Patent Application Serial No. 60/329,469, filed Oct. 8, 2001, which is hereby incorporated by reference in its entirety.

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Summary of Invention Paragraph - BSTX (18):

[0016] Further, a method is provided for collecting light emissions with high efficiency through a low cost lens element in an SIL configuration. An object to be observed is immersed in fluid and positioned in alignment with the solid immersion lens portion so that the object is within a field of light collection extending through very large numerical aperture spherical solid immersion lens portion. The object, immersed in a fluid of high index of refraction, emits observable optical energy typically by **fluorescence** in response to excitation, and the emissions at selected wavelengths are collected through the spherical solid immersion lens portion of an even higher index of refraction and directed to a sensor, typically without imaging, so that the emissions can be measured. The structure admits to high collection efficiency. Once again, the use of the meniscus type lens in combination with the SIL lens structure further enhances the obtained benefits.

Detail Description Paragraph - DETX (21):

[0071] FIG. 6 is illustrative of a light collection system 200 employing an SIL 50 in accordance with the invention. An example is a cytometer or a highly efficient spectrometer. The system 200 includes a laser 210 projecting a beam 211, an expansion lens 212, a first collimating lens 214, an optional first dichroic filter 217 selected for passing the selected output wavelength of the laser 210, a partially transmissive mirror 216, a second collimating lens 218, an SIL structure 50, a second dichroic filter 219 selected for passing the selected emission of the sample, a collection lens 220, a photon collection device such as a photomultiplier tube 226 and a control apparatus 223. In operation, the laser 210 projects an illumination beam 211 through expansion lens 212 and collimating lens 214 to produce a broad coherent monochromatic illumination beam 215. Its purity is further selected by filter 217 so that the illumination can be used as an excitation probe. The beam 215 is reflected by mirror 216 to second collimating lens 218 through which it is focused through an air medium to the SIL structure 50. Focus adjustment is by means of positioning of the second collimating lens 218 relative to the SIL structure 50. However, as an emission collection apparatus, imaging is not the goal. The SIL structure 50 further concentrates the illumination to in the sample chamber (not shown) within the body portion, in immersion contact with the lens. The sample is excited by the illumination and positioned by the control apparatus 223. (The control apparatus 223 may both position a platform and supply the object or sample to be viewed.) The illumination excites the sample to cause it to emit **fluorescent** energy which is collected by the high numerical aperture lens and is directed back through the second collimating lens 218 which focuses to infinity and directs the emitted photonic energy through the half silvered mirror 216 to the second filter 219, which blocks any stray excitation, and then through the third collimating lens 220. The third collimating lens 220 concentrates the photonic energy into a collection region of a photon sensor such as a photomultiplier tube (PMT) 226. The relative positioning of the lens 120 and the PMT 226 the collection efficiency. This application is believed to be a new application of an SIL structure. Other configurations may be employed as suggested by this configuration. Significantly, the SIL structure 50, although an essential element of the optical system is obtained from a manufacturing process which yields extremely inexpensive optical elements as compared to conventional lenses, so the SIL structure 50, which is integral with the sample carrier, is disposable. This is believed to be a significant advance over conventional SIL technology.

Detail Description Paragraph - DETX (25):

[0075] A method for producing the SIL structure 300 is described with reference to FIGS. 8 through 16. Referring to FIG. 8, a substrate 330 is provided and includes a first surface 332 and an opposing second surface 333. The first surface 332 should be of a planar construction and in one exemplary embodiment, the substrate 330 is a silicon wafer or other rigid structure. The substrate 330 functions as a foundation for fabrication of a mold which is used to form the SIL structure 300. Preferably, the substrate 330 undergoes conventional cleaning operations to ensure that it is of high quality and without foreign matter. To form the mold, a first layer 334 of moldable material from which the mold is to be formed is cast on the first surface 332 of the substrate 330, as shown in FIG. 9. The first layer 334 is preferably formed to have a uniform thickness and is free of any imperfections such as **bubbles**, etc. Suitable techniques, such as spin coating, are preferably used so as to create a uniform thickness for the first layer 334 and remove any imperfections. The first layer 334 is then permitted to set. In one exemplary embodiment, the first layer 334 is of a pliant material, such as a room temperature vulcanization (RTV) elastomer. One particularly preferred RTV is commerically available under the trade name RTV 615 from General Electric.

Detail Description Paragraph - DETX (51):
[0099] The material from which the mold is to be formed (in this case silicon) is preferably prepared a maximum of 4 hours before use, complete manufacturing takes about this amount of time so the silicon is mixed immediately before beginning. To prepare 30 grams of 10:1 silicon, mix the two components (27 grams of GE RTV 615A and 3 grams of GE RTV 615B) and use an Eyence Hybrid Mixer (mix for 1 minute and defoam for 2 minutes). If some bubbles appear when pouring RTV, it's helpful to defoam again for 1 or 2 minutes.

Detail Description Paragraph - DETX (53):
[0101] To make a first layer of RTV, pour fresh RTV on the substrate locked by a vacuum. Completely cover the substrate and remove the bubbles with a wood tongue depressor. Then, launch the spin coater at 700 RPM for 1 minute, with two ramps of 15 seconds. After spinning, place the cover slip in a covered petri dish and bake for 3 minutes at 80.degree. C.

Detail Description Paragraph - DETX (59):
[0107] The substrate is then placed in a petri dish, at 1 cm from the bottom of the dish using a wood tongue depressor, and an excess of silicon is poured in. The bottom of the substrate should be free from any silicon. It's very difficult to fill the hole with silicon without using vacuum, so the petri dish has to be placed in the degassing machine for an average of 20 minutes. All the bubbles should disappear from the surface of the mold. The substrate is placed into the spin coater and spun at 700 RPM for 1 minute, with two ramps of 15 seconds: this will create a flat surface, with the right thickness for the lens. The substrate is then placed in a new petri dish and cooked for 45 minutes at 80.degree. C.

Detail Description Paragraph - DETX (85):
[0132] The petri dish is taken out of the oven, and is cooled for a few minutes. Then treat it with oxygen plasma for 2 minutes and pour some new silicon. The thickness of this new layer doesn't need to be perfectly known, it just has to be thick enough to be rigid; preferably the layer is at least about 5 mm thick. The use of the degassing machine is preferred to prevent micro-bubbles that can appear during curing. The dish is heated for at least 1 hour, then it is cooled.

Detail Description Paragraph - DETX (89):
[0136] On both sides of the mold, separately, pour an excess of fresh silicon. Use the degassing machine to take the bubbles out of the hole of the upper layer.

Detail Description Paragraph - DETX (95):
[0142] Referring to FIG. 7 and FIG. 17, the SIL structure 300 may be used in the same applications that were mentioned with respect to the SIL structure 50. For example, the SIL structure 300 may be used in conventional imaging systems, including miniature microscope applications and the SIL structure 300 may further be used in light collection systems, such as a cytometer or a highly efficient spectrometer. A further application for the SIL structure 300 is in the form of arrays of lenses to enhance fluorescence detection, associated with screening micro-arrays. These arrays can be used to improve collection efficiency for CCDs. Because the SIL structure 300 acts not only as an

efficient collector of light but also as an efficient means for concentrating and focusing light, its potential applications are widespread.

Detail Description Paragraph - DETX (99):

[0146] It will be appreciated that there are a wide range of applications for a system using the SIL lens structure/meniscus type lens combination. For example, this combination demagnifies an incident spot of light by a factor of 4 due to its optical properties. This characteristic can be exploited to improve the performances of CD burners and/or data storage and have utility in photolithography applications. The lens combination also significantly improves the light collection available with simple optical elements in a very cost effective production process and at low material costs. For example, one application is arrays with collection optics that send light to infinity. The array can be screened with a simple optical apparatus that doesn't require a precise positioning along a vertical axis. The mobile head that reads the fluorescence for example can be lighter than conventional apparatuses.

Detail Description Paragraph - DETX (100):

[0147] Other potential applications using the SIL structure 300 combined with the meniscus type lens 400 include the following: (1) a cell sorter and other applications that need a fluorescence detection or even just light detection; (2) a microscope that is micro-sized so that it can be placed on the top of an optical fiber; in addition, an endoscope can be designed to include an integrated microscope; and in general the lenses can be arranged such that they allow detection and function as a microscope in places unreachable with conventional microscopes; (3) microspectrophotometer with integration of a grating/prism; (4) a system that measures the coefficient of diffusion in liquids with a high precision; furthermore, by using a technique called fluorescence recover after photobleaching, the exact size of particles diffusing in a liquid can be determined and perhaps the affinities between proteins can be calculated; (4) an efficient confocal microscope; (5) using evanescent waves (created by prism, through the objective or using a stretched optical fiber), single molecule detection may be possible; and (6) the combination of techniques such as fluorescence recovery spectroscopy and evanescent waves can lead to a very efficient inspection of liquid medias: molecules near surfaces, concentration and interaction with a surface carrying other molecules; moreover, a chip can be designed to screen the interactions and automate drug affinity characterization.

Detail Description Paragraph - DETX (123):

[0170] The ability to produce conventional lenses of any shape in a cost effective manner is attractive to manufacturers of a wide array of products. For example, many toy producers have product lines that incorporate some type of conventional lens into the product. These products range from simple beginner microscopes and simple goggles to more complex optical containing products. The present lens manufacturing methods can be used to produce complex optical components, such as camera/video objectives. In addition, it is possible to realize switchable objectives for disposable cameras even those having wide angles. Currently, the disposable cameras that are commercially available are not entirely disposable as the objectives of the camera are typically reused. Using elastomeric lenses not only reduces the cost of the product but also makes the product completely disposable. Moreover, the ability to produce objectives for panoramic pictures at reasonable prices is very appealing.

Detail Description Paragraph - DETX (131):

[0178] An SIL or mensicus type combination lens provides high numerical aperture (NA) to and from an electro-optic device fabricated within a semiconductor or microfluidics chip or any other suitable structure capable of incorporating optical sources and detectors, such as LEDs, laser diodes, photodiodes, avalanche photodiodes, or any other type of light source or detector. High numerical aperture (NA) coupling is beneficial for coupling light from samples since the collection efficiency is proportional to NA.sup.4 for fluorescence detection and NA.sup.2 for luminescence detection.

Detail Description Paragraph - DETX (137):

[0184] Referring to FIG. 49, mold cores 1320 are then set into the wells 1330. The mold cores 1320 can be formed of sapphire, ruby, or steel and are in the form of spheres. The mold cores 1320 rest on the substrate 1300 with the photoresist layer 1310 contacting the mold cores 1320 at select points. The exposed surfaces of the mold cores 1320 and the photoresist layer 1310 form a well-defined boundary. The greater the mold cores 1320 protrude above the photoresist layer 1310, the greater the undercut regions of the mold will be. To form the mold, a moldable material (e.g., silicon elastomer) is cast onto the surface defined by the protruding mold cores 1320 and the exposed photoresist layer 1310 to define a first layer 1340 as shown in FIG. 50. Preferably care is taken so that small bubbles are not trapped in crevices at the intersection of the mold cores 1320 and the photoresist layer 1310. One preferred method for their removal is placing the entire structure into a vacuum for minutes. The thickness of layer 1340 should completely submerge the mold cores 1320 and supply mechanical stiffness. Once the layer 1340 is set by curing, the layer 1340 is removed along with the mold cores 1320 and the layer 1340 is treated with oxygen plasma. The layer 1340 has a series of defined cavities 1342.

Detail Description Paragraph - DETX (142):

[0188] By using one of the solid immersion lens structures disclosed herein, the numerical aperture (NA) of the optical system may be increased to a value that is otherwise not obtainable using conventional lenses. FIG. 54 illustrates how the NA is increased using a solid immersion lens. An optical system 1400 is illustrated and in the exemplary embodiment, the system 1400 is a fluorescent microscope arrangement. The set of filters is chosen according to the dyes used in the different experiments (blue excitation and green emission). A laser 1410 is used to create the excitation and in this instance the laser 1410 is a blue laser having a wavelength of 488 nm and a beam diameter of 1 mm. A number of companies manufacture lasers having these characteristics and one exemplary laser 1410 is a Uniphase 2214-10 SL Argon Laser. The excitation may also be created by a blue LED 1220, e.g., Luxeon Star/C.

Detail Description Paragraph - DETX (143):

[0189] The filter set is selected in view of the excitation wavelength (coming from the laser 1410 or the blue LED 1420 and allows only the fluorescent emission to be focused on an image detector 1430, such as a CCD camera. The beam of the laser 1410 is increased with first and second lenses 1440, 1450, respectively. The lenses 1440, 1450 have a diameter of 1.9 cm and focal lengths of -2 cm and 4 cm, respectively. The beam is then filtered by an excitation filter 1460 (wavelength of 465 nm to 495 nm) and is reflected by a dichroic filter 1470 towards a lens 1480 that focuses the beam on the solid immersion lens 300. It will be appreciated that the solid immersion lens 300 is formed according to one of the molding methods disclosed herein. In one

exemplary embodiment, the lens 1480 has a diameter of 1.9 cm and a focal length of 1.15 cm. The lens 1480 is chosen that the initial NA, with the SIL 300, is high (NA=0.65). The blue LED 1420 is arranged so that it is the focal point of a first lens 1490 (diameter 1.9 cm and focal length 3 cm) so that the excitation is able to filtered by an excitation filter 1500 (wavelength 470 nm to 490 nm). A second lens 1510 (diameter 1.9 cm and focal length 1.15 cm) is arranged to focus the rays on the passage (i.e., observation region 310 of FIG. 7) under the lens portion of the SIL 300.

Detail Description Paragraph - DETX (144):

[0190] FIG. 55 illustrates the excitation wavelength of the above-described set of lenses which is selected to allow only the fluorescent emission to be focused on a CCD camera or the like.

Detail Description Paragraph - DETX (147):

[0193] In order to measure the numerical aperture, fluorescent beads (Interfacial Dynamics Corporation 2-FY-1K.2) of diameter 5 microns, an excitation wavelength of 490 nm, an emission wavelength of 515 nm, a concentration of 2.times.10.sup.8 beads per ml to measure the numerical aperture of the SIL structure 300.

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INVENTOR-INFORMATION:

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RELATED-US-APPL-DATA:

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parent continuation-in-part-of 09517230 20000302 US PENDING

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parent-patent 6117176 US

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parent continuation-in-part-of PCT/US97/17534 19970930 US PENDING

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child 08665343 19960617 US

parent continuation-in-part-of PCT/US94/04278 19940419 US PENDING

child 08665343 19960617 US

parent continuation-in-part-of PCT/US94/07314 19940627 US PENDING

child 08665343 19960617 US

parent continuation-in-part-of 08288690 19940811 US GRANTED

parent-patent 5633286 US

child 08665343 19960617 US

parent continuation-in-part-of 08581188 19951229 US ABANDONED

child 08665343 19960617 US

parent continuation-in-part-of 08581191 19951229 US GRANTED

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child 08665343 19960617 US

parent continuation-in-part-of 08581125 19951229 US GRANTED

parent-patent 5962572 US

child 08581188

parent continuation-in-part-of PCT/US94/07314 19940627 US PENDING

child 08581188

parent continuation-in-part-of PCT/US94/04278 19940419 US PENDING

child 08581191

parent continuation-in-part-of PCT/US94/07314 19940627 US PENDING

child 08581191

parent continuation-in-part-of PCT/US94/04278 19940419 US PENDING

child 08581125

parent continuation-in-part-of PCT/US94/07314 19940627 US PENDING

child 08581125

parent continuation-in-part-of PCT/US94/04278 19940419 US PENDING

US-CL-CURRENT: 310/309

ABSTRACT:

Novel gels and articles are formed from one or more copolymers having at least one poly(ethylene) components and high levels of one or more plasticizers, said gels having an amount of crystallinity, glassy components, and selected plasticizers sufficient to achieve improvements in one or more physical properties including improved crack propagation resistance, improved tear resistance, improved resistance to fatigue, resistance to catastrophic failure, and exhibiting high strain under elongations not obtainable in amorphous gels which high strain making the gel suitable for use as film layers for artificial muscles.

RELATED APPLICATIONS

[0001] This application is a continuation-in-part of the following applications: Ser. No. 09/517/230, filed Mar. 2, 2000, Ser. No. 09/412,886, filed Oct. 5, 1999, Ser. No. 09/285809, filed Apr. 1, 1999 Ser. No. 09/274498, filed Mar. 23, 1999; Ser. No. 08/130,545, filed Aug. 8, 1998, Ser. No. 08/984,459, filed Dec. 3, 1997, Ser. No. 08/909,487, filed Jul. 12, 1997; Ser. No. 08/863,794, filed May 27, 1997; PCT/US97/17534, filed Sep. 30, 1997, U.S. Ser. No. 08/719,817 filed Sep. 30, 1996, U.S. Ser. No. 08/665,343 filed Jun. 17, 1996 which is a Continuation-in-part of U.S. Ser. No. 612,586 filed Mar. 8, 1996, PCT/US94/04278 filed Apr. 19, 1994 (published May 26, 1995 No. WO95/13851); PCT/US94/07314 filed Jun. 27, 1994 (published Jan. 4, 1996 No. WO 96/00118), Ser. No. 288,690 filed Aug. 11, 1994, Ser. No. 581,188 filed Dec. 29, 1995, Ser. No. 581,191 filed Dec. 29, 1995 Ser. No. 5,81,125 filed Dec. 29, 1995 now U.S. Pat. No. 5,962,527 In turn U.S. Ser. Nos. 581,188; 581,191, and 581,125 (now U.S. Pat. No. 5,962,572) are continuation in-parts of the following applications Ser. Nos. 288,690, filed Aug. 11, 1994, PCT/US94/07314 filed Jun. 27, 1994 (CIP of PCT/US 94/04278, filed Apr. 19, 1994) The subject matter contained in the related applications and patents are specifically incorporated herein by reference

---------- KWIC ---------

Detail Description Paragraph - DETX (61):
[0076] The gels of the invention can be formed into gel strands, gel tapes, gel sheets, films, and other articles of manufacture in combination with or

without other substrates or materials such as natural or synthetic fibers, multifibers, fabrics, films and the like. Moreover, because of their improved tear resistance and resistance to fatigue, the gels exhibit versatility as balloons for medical uses, such as balloon for valvuloplasty of the mitral valve, gastrointestinal balloon dilator, esophageal balloon dilator, dilating balloon catheter use in coronary angiogram and the like. Since the gels are more tear resistant, they are especially useful for making condoms, toy balloons, and surgical and examination gloves. As toy balloons, the gels are safer because it will not rupture or explode when punctured as would latex balloons which often times cause injures or death to children by choking from pieces of latex rubber. The gels are advantageously useful for making gloves, thin gloves for surgery and examination and thicker gloves for vibration damping which prevents damage to blood capillaries in the fingers and hand caused by handling strong shock and vibrating equipment. The gels are also useful for forming orthotics and prosthetic articles such as for lower extremity prosthesis described below.

Detail Description Paragraph - DETX (70):

[0085] The gels of the invention can be formed into gel strands, gel bands, gel tapes, gel sheets, and other articles of manufacture in combination with or without other substrates or materials such as natural or synthetic fibers, multifibers, fabrics, films and the like. Moreover, because of their improved tear resistance and resistance to fatigue, the gels exhibit versatility as balloons for medical uses, such as balloon for valvuloplasty of the mitral valve, gastrointestinal balloon dilator, esophageal balloon dilator, dilating balloon catheter use in coronary angiogram and the like. Since the gels are more tear resistant, they are especially useful for making condoms, toy balloons, and surgical and examination gloves. As toy balloons, the gels are safer because it will not rupture or explode when punctured as would latex balloons which often times cause injures or death to children by choking from pieces of latex rubber. The gels are advantageously useful for making gloves, thin gloves for surgery and examination and thicker gloves for vibration damping which prevents damage to blood capillaries in the fingers and hand caused by handling strong shock and vibrating equipment. Various other gel articles can be made from the advantageously tear resistant gels and gel composites of the inventions include gel suction sockets, suspension belts.

Detail Description Paragraph - DETX (185):

[0191] If the amount of a gas in oil exceeds saturation, small bubbles will form, remain suspended, and the oil will appear hazy This is called entrained gas. The bubbles slowly rise to the surface Bubbles of a gas, such as air, in an oil film cause holes that reduce oil film continuity and decrease the film's ability to prevent solid-to-solid contact.

Detail Description Paragraph - DETX (186):

[0192] The relative tendency of various oils to release entrained gas is measured by a gas bubble separation method ASTM D 3427. The method uses a cylinder-like test vessel with gas inlet and outlet ports. Air, or another gas (if of interest), is introduced into the bottom of the vessel at a specified temperature and flow rate. At the end of seven minutes the gas flow is stopped and the change in density as measured by a densitometer is recorded. The test is complete when the total volume of entrained air is reduced to 0.20% by volume. The results are reported as the time it took for the oil to attain this value.

Detail Description Paragraph - DETX (187):

[0193] Foaming is defined as the production and coalescence of gas bubbles on a lubricant surface. Foam may be a result of a variety of problems including air leaks, contamination, and over filling of sumps. Foaming can cause loss of oil out of a vent and serious operational problems in most lubricated systems. Excessive foam can starve bearings and pumps of liquid lubricant (pump cavitation) causing failure, and cause poor performance in hydraulic systems. The foaming characteristics of an oil are measured by ASTM D-892. Using a calibrated porous stone, air is blown into the bottom of a graduated cylinder for a specified time. Immediately upon completion of the blowing period, the foam that has formed on the top of the oil is measured. Ten minutes after the completion of the blowing period, an additional measurement is made of the remaining foam as the foam retention characteristics of the oil. The results are reported in milliliters.

Detail Description Paragraph - DETX (225):

[0231] The present invention gel can also contain useful amounts of conventionally employed additives such as stabilizers, antioxidants, antiblocking agents, colorants, fragrances, flame retardants, flavors, other polymers in minor amounts and the like to an extend not affecting or substantially decreasing the desired properties. Additives useful in the gel of the present invention include: tetrakis[methylene3,-(3'5'-di-t-ertbutyl4"-hydroxyphenyl) propionate] methane, octadecyl 3-(3",5"-di-tert-butyl-4"-hydroxyphenyl) propionate, distearyl-pentaerythritol-diproprionate, thiodiethylene bis-(3,5-ter-butyl-4-hydrox- y) hydrocinnamate, (1,3,5-trimethyl-2,4,6-tris[3,5-di-tert-butyl-4-hydroxy-benzyl] benzene), 4,4"-methylenebis(2,6-di-tert-butylphenol), Tinuvin P, 123, 144, 213, 234, 326, 327, 328, 571, 622, 770, 765, Chimassorb 119, 944, 2020, Uvitex OB, Irganox 245, 1076, 1098, 1135, 5057, HP series: 2215, 2225, 2921, 2411, 136, stearic acid, oleic acid, stearamide, behenamide, oleamide, erucamide, N,N"-ethylenebisstearamide, N,N"-ethylenebisoleamide, sterryl erucamide, erucyl erucamide, oleyl palmitamide, stearyl stearamide, erucyl stearamide, calcium sterate, other metal sterates, waxes (e.g. polyethylene, polypropylene, microcrystalline, carnauba, paraffin, montan, candelilla, beeswax, ozokerite, ceresine, and the like). The gel can also contain metallic pigments (aluminum and brass flakes), TiO2, mica, fluorescent dyes and pigments, phosphorescent pigments, aluminatrihydrate, antimony oxide, iron oxides (Fe3O4, --Fe2O3, etc.), iron cobalt oxides, chromium dioxide, iron, barium ferrite, strontium ferrite and other magnetic particle materials, molybdenum, silicone fluids, lake pigments, aluminates, ceramic pigments, ironblues, ultramarines, phthalocynines, azo pigments, carbon blacks, silicon dioxide, silica, clay, feldspar, glass, microspheres, barium ferrite, wollastonite and the like The report of the committee on Magnetic Materials, Publication NMAB-426, National Academy Press (1985) is incorporated herein by reference

Detail Description Paragraph - DETX (241):

[0247] The invention gels are prepared by blending together the components (I, II, or III) including the various additives as desired at about 23.degree. C. to about 100.degree. C. forming a paste like mixture and further heating said mixture uniformly to about 150.degree. C. to about 200.degree. C. until a homogeneous molten blend is obtained. Lower and higher temperatures can also be utilized depending on the viscosity of the oils and amounts of multiblock copolymers (I) and polymer (III) used. These components blend easily in the melt and a heated vessel equipped with a stirrer is all that is required Small batches can be easily blended in a test tube using a glass stirring rod for mixing. While conventional large vessels with pressure and/or vacuum means can

be utilized in forming large batches of the instant compositions in amounts of about 40 lbs or less to 10,000 lbs or more. For example, in a large vessel, inert gases can be employed for removing the composition from a closed vessel at the end of mixing and a partial vacuum can be applied to remove any entrapped bubbles. Stirring rates utilized for large batches can range from about less than 10 rpm to about 40 rpm or higher.

Detail Description Paragraph - DETX (242):

[0248] The invention gel can also contain gases as an additive, i.e. the gel can be foamed. Foam is herein defined as tightly or loosely packing aggregation of gas bubbles, separated from each other by thin or thick layers of gel. Many types of foamed invention gels (from ultra high density to ultra low density) can be produced as desired by (i) adding gas to the molten gel during processing, and (ii) producing gas in the molten get during processing. Gas can be added by whipping a gas into the molten gel before it cools or introduce a gas into the molten gel and then expand or reduce the size of the gas bubbles by reducing the pressure to reduce the bubbles size or applying high pressure to expand the bubbles size. In this regard, inert gases such as Carbon dioxide, Nitrogen, Helium, Neon, Argon, Krypton, Xenon and Radon are suitable. Air can also be used. Gas can be produced in the molten gel by adding one or more of a "blowing agent" to the Useful blowing agents include dinitroso compounds, such as dinitroso pentamethylene-tetramine, azodicarbonamide, 4,4'oxybis(benzenesulfonyl) hydrazine, 5-phenyltetrazole, p-toluenesulfonyl semicarbazide, sulfonyl hydrazide, such as benzene sulfonylhydrazide. Water can be used as a "blowing agent" to .sup.1 produce varying density of foam invention gels; water used to advantage can be in the form of mist, droplets, steam, and hot or cold water. The density of the foam invention gels can vary from less than 1.00 kilograms per cubic meter to near the solid gel density. Although the materials forming soft solid invention gels may be more shear resistant, the same materials when made into a foam become much less shear resistant

Detail Description Paragraph - DETX (246):

[0252] As the invention gels formed from multiblock copolymers (I) having more and more midblock polymer chains can be expected to exhibit greater delay recovery form extension or longer relaxation times with increasing number of midblocks and increasing midblock lengths, such invention gels having more than three midblocks forming the copolymers (I) can exhibit extreme tear resistance and excellent tensile strength while at the same time exhibit almost liquid like properties. For example, a fun toy can be made from (S-E-EB-E-S), (S-B-EB-EB-S), (S-E-EP-E-EP-S), (S-P-EB-P-EB-S), (S-E-EB-E-EB-E-S), (S-E-EP-E-EP-E-EP-E-S), (S-E-EP-EP).sub.n, (S-B-EP-E-EP).sub.n, (S-E-EP-E-EP-E).sub.n, (S-E-EB-E-EB-E-EB-E-EB-S).sub- .n copolymer invention gels which are molded into cube shapes when placed on the surface of a incline will collect it self together and flow down the incline as a moving body much like a volume of water moving on a high surface tension surface. This is due to the greater distance between the end block (A) domains. Such liquid like performing invention gels can be very strong and exhibit extreme tear resistance as exhibited by invention gels made from (S-E-EP-S) multiblock copolymer invention gels with shorter (A) distance between domains. Such liquid like invention gels when shaped into a cube will be deformed by the force of gravity on Earth, but will retain its memory and regain to its molded cube shape when released in outer space or reform into a cube if let loose in a container of liquid of equal density. As a comparison, such a toy formed in the shape of a large cube from a high viscosity triblock copolymer with a plasticizer content of 1:1,600 parts will be flattened by the force of gravity and run down an incline, but is very fragile and will start to tear if attempt

is made to pick it up by hand. This is an excellent comparison of the difference of tear resistance difference between triblock copolymer gels and multiblock copolymer invention gels. A useful application is to use such an elastic liquid gel volume to fill a container or to encapsulate an electrical or electronic component in a container filling every available space, when needed, the shapeless gel volume can be removed by pouring it out of the container whole.

Detail Description Paragraph - DETX (255):

[0261] The invention gel can be formed into gel strands, gel bands, gel tapes, gel sheets, and other articles of manufacture in combination with or without other substrates or materials such as natural or synthetic fibers, multifibers, fabrics, films and the like. Moreover, because of their improved tear resistance and resistance to fatigue, the invention gels exhibit versatility as balloons for medical uses, such as balloon for valvuloplasty of the mitral valve, gastrointestinal balloon dilator, esophageal balloon dilator, dilating balloon catheter use in coronary angiogram and the like. Since the invention gels are more tear resistant, they are especially useful for making condoms, toy balloons, and surgical and examination gloves. As toy balloons, the invention gels are safer because it will not rupture or explode when punctured as would latex balloons which often times cause injures or death to children by choking from pieces of latex rubber. The invention gels are advantageously useful for making gloves, thin gloves for surgery and examination and thicker gloves for vibration damping which prevents damage to blood capillaries in the fingers and hand caused by handling strong shock and vibrating equipment. Various other gel articles can be made from the advantageously tear resistant invention gels and invention gel composites of the inventions include gel suction sockets, suspension belts,

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TITLE: Renilla reniformis fluorescent proteins, nucleic acids encoding the fluorescent proteins and the use thereof in diagnostics, high throughput screening and novelty items

PUBLICATION-DATE: May 15, 2003

US-CL-CURRENT: 435/69.1, 530/350

APPL-NO: 09/ 808898

DATE FILED: March 15, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60189691 20000315 US

RELATED APPLICATIONS

[0001] Benefit of priority under 35 U.S.C. .sctn.119(e) is claimed to U.S. provisional application Serial No. 60/189,691, filed Mar. 15, 2000, to Bryan et al., entitled "RENILLA RENIFORMIS FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS" is claimed.

[0002] This application is related to allowed U.S. application Ser. No. 09/277,716, filed Mar. 26, 1999, to Bruce Bryan and Christopher Szent-Gyorgyi, entitled "LUCIFERASES, FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE LUCIFERASES AND FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS." This application is related to International PCT application No. WO 99/49019 to Bruce Bryan and Prolume, LTD., entitled "LUCIFERASES, FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE LUCIFERASES AND FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS."

[0003] This application is also related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS", now U.S. Pat. No. 5,876,995, issued Mar. 2, 1999, and in U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASTIC TISSUE AND OTHER TISSUES". The application is also related to U.S. application Ser. No. 08/990,103, filed Dec. 12, 1997, to Bruce Bryan entitled "APPARATUS AND METHODS FOR DETECTING AND IDENTIFYING INFECTIOUS AGENTS".

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DOCUMENT-IDENTIFIER: US 20030090893 A1

TITLE: Lighting system and device

PUBLICATION-DATE: May 15, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Nepil, James	Garfield	NJ	US	

APPL-NO: 10/ 005761

DATE FILED: November 12, 2001

US-CL-CURRENT: 362/101, 362/235 , 362/318 , 362/800 , 362/96

ABSTRACT:

The present invention is a light-producing technology exemplified by lighting that is safe, reliable, energy efficient, long lasting, and capable of operating under a wide range of weather and other conditions. The device incorporates a durable housing, a light element, a liquid solution, and a power supply. Subject only to its power source, it is capable of indefinitely producing intensely visible light at 100 yards or more during both daytime and nighttime. It can be configured for higher or lower intensities in a wide variety of foreseen applications. The device is not flammable, explosive, or toxic, and without loss of function withstands shock, extended water immersion, and heating and cooling to temperatures below freezing and approaching boiling.

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Summary of Invention Paragraph - BSTX (9):

[0007] The device of U.S. Pat. No. 4,967,321 to Cimock is a flashlight wand designed as a children's toy. The wand contains two DC batteries, a small incandescent bulb, and light reflecting objects. Light production of the Cimock device is limited. U.S. Pat. No. 5,392,203 to Harris, Jr. discloses a waterproof taxi light to guide aircraft on a tarmac. The device includes a lighted signal member with an elongate, translucent tubular member adapted for providing both daytime and nighttime illumination. The light source is a DC battery powered flashlight bulb. The translucent tube provides for light dispersion. Harris, Jr. discloses the use of a clear fluid within the translucent tubular member (column 6, lines 10-15), but the light element, a bulb, is not even partially submerged in the fluid. Thus, the light is not as intense as it could be if the light element were at least partially submerged in the fluid.

Summary of Invention Paragraph - BSTX (11):

[0009] U.S. Pat. No. 4,070,777 to Lo Giudice discloses a novelty display device incapable of producing intensely visible light. Designed for amusement, this device uses miniature lamps strung through the length of a liquid-filled housing to illuminate a continuous flow of bubbles through a liquid contained within a hollow glass tube. Boiling liquid heated by lighted bulbs is the

bubble source. The device is not only an inadequate means of producing high intensity lighting, but it is also not durable because the glass housing will likely shatter if dropped. U.S. Pat. No. 4,271,458 to George, Jr. discloses decorative light tubing for lighted tube displays. The device comprises a flexible tube containing a dielectric fluid (such as mineral oil or glycerin) and low voltage filament bulbs. However, this device is incapable of producing high-intensity lighting.

Summary of Invention Paragraph - BSTX (12):

[0010] U.S. Pat. No. 4,600,974 to Lew et al. discloses an optically decorated light baton with multiple purposes similar to the present prototype. It is a portable light tube with reflective platelets suspended in a medium, and in one embodiment phosphorescent or fluorescent material coats the light-emitting tube. The device of U.S. Pat. No. 5,165,781 to Orak is a novelty flashlight with color producing chambers intended for use as a toy or amusement. It comprises a low heat generating filament bulb and colored-fluid-containing transparent cups mounted to a power receiving housing. The light is not intensely visible because the bulb is at one end of the housing, which itself lacks fluid. The device requires continuous agitation to swirl the liquid colors. Although the housings of these two devices are fluid-filled, the light is not intensely visible partly because the light sources are located at only one end of the device where there is no fluid. Furthermore, although both devices utilize fluid mediums, both require agitation to obtain the full effect of the fluid: the Orak device requires agitation to swirl the liquid colors and the Lew et al. device requires agitation to make the light reflecting particles move through the fluid.

Summary of Invention Paragraph - BSTX (13):

[0011] U.S. Pat. No. 5,662,406 to Mattice discloses a lighted baby bottle designed for easy location in the dark. A filament bulb produces a low intensity glowing light and some heat. U.S. Pat. No. 5,993,021 to Lin discloses a decorative lamp designed for aquarium accent lighting. A tube containing water and artificial fish is illuminated by a low-intensity, heat-producing filament bulb not immersed in the fluid. A bubble valve produces air bubbles which cause the artificial fish to move.

Summary of Invention Paragraph - BSTX (19):

[0016] Briefly described, in a preferred form, the present invention comprises a new light-generating technology, and lighting devices that incorporate the technology. The light-generating technology incorporates the use of a fluorescent dye dissolved in a fluid medium that at least partially surrounds the light element. The preferred lighting device utilizing this lighting principal comprises a durable housing, a light element, a power source for the light element, and a lighting fluid at least partially surrounding the light element.

Summary of Invention Paragraph - BSTX (20):

[0017] The device is lightweight, safe, durable, long lasting, and energy efficient. The present lighting device incorporates the following characteristics, among others, which distinguish the invention from the prior art: (a) the new lighting principle--fluorescent dye dissolved in a fluid medium; (b) high energy efficiency--high light intensities generated by low power (AC or DC); (c) long operational life--subject only to power supply, light emission continues indefinitely without chemical breakdown or materials fatigue; (d) adjustable light intensity--by composition of the fluid medium and

control of the power source; (e) simple construction--few parts to fail; and (f) durable construction--water-submersible and shock-proof, virtually unbreakable in normal use.

Summary of Invention Paragraph - BSTX (22):

[0019] The light-emitting section comprises an LED secured to the housing and at least partially submerged in a lighting fluid. In a preferred form, the device comprises four LEDs for sufficient light intensity, and the lighting fluid comprises a solution of approximately 10 ml water, 7 ml of 80 proof vodka as a non-toxic ethanol source, and 5 ml of water-soluble, non-toxic, fluorescent color from Createx Colors of East Granby, Conn. The lighting fluid preferably fills approximately 7/8ths of the light-emitting section, leaving approximately 1/8.sup.th of the section as air space. Coolants of the lighting fluid can be other than alcohol, for example de-icing fluid Types 1 and 4. While these are toxic, they can be used with or without aqueous dilution with water. It will be understood by those of skill in the art that ingredient concentrations can vary to produce different effects and intensities, although some combinations may have disadvantageous effects. For example, as more color is used, the more likely it is to adhere to the LEDs, causing a rise in temperature.

Summary of Invention Paragraph - BSTX (26):

[0023] The present invention is superior to prior art devices in numerous ways. The following examples are specific distinguishing features of the present invention and the above-described prior art. The present invention differs from the Harris, Jr. light in its use of LEDs in a fluorescing fluid as an integral part of a lighting principle. The Harris, Jr. device is not submergible, nor as durable as the present invention. The present devices differ from that of Harris, Jr. in that their body is filled with a mixture of ethanol, water, and fluorescent dye, and has LEDs as the light source. The LEDs are pushed to a controllably higher voltage limit than they were designed for because the fluid serves as a coolant in addition to dispersing the light. The filament bulb of the Harris, Jr. device draws high power vs. that of the present devices' LEDs, but emits a much lower intensity of usable light. Compared to light bulbs, LEDs are less subject to breakage in use and have a far longer life span. In fact, the design of the present invention was prompted by use of a Harris, Jr. type device under harsh airport conditions where it failed under temperature extremes, and broke when dropped or exposed to vibration. Harris, Jr. discloses that a clear liquid could be used in its fluidless device, but the reason for this is unclear as the bulb of Harris, Jr. would fail under immersion. Finally, the Harris, Jr. design has limited use, not the broad applications foreseen for the technology of the present application.

Summary of Invention Paragraph - BSTX (27):

[0024] The Lew et al. device differs from the present invention in having incandescent vs. LED light sources, reflective platelets in the medium, a phosphorescent or fluorescent surface coating (if present) vs. dissolved in the fluid, and it must be agitated or mixed during use to make the light reflecting particles move through the medium. Further, only low light intensities are generated.

Summary of Invention Paragraph - BSTX (32):

[0029] An object of the present invention is to disclose a new lighting principle--fluorescent dye dissolved in a fluid medium;

Detail Description Paragraph - DETX (7):

[0041] In one preferred embodiment, the lighting fluid 40 is a solution often (10) parts of water, seven (7) parts of 80-proof vodka, and five (5) parts of water-soluble, non-toxic, fluorescent color from Createx Colors. However, the concentrations can be varied. Alternatively, as will be understood by those of skill in the art, other materials such as glycol, salt, and isopropyl alcohol can be used. Preferably, the lighting fluid 40 contains no particulate matter so the emitted light is not reflected or refracted in the lighting fluid 40. However, the lighting fluid 40 can contain other material, whether soluble or not. Alternatively, the lighting fluid 40 can be other gaseous or liquid substance or any combination of such substances that provide some element of durability to the device 10 and/or additional luminosity. The lighting fluid 40 preferably fills 7/8ths of the light-emitting section 24, leaving 1/8th as air space. However, these proportions can be varied.

Claims Text - CLTX (10):

9. The lighting device of claim 8, wherein the coolant selected from the group consisting of ethanol and de-icing fluid Types 1 and 4, and wherein the color is fluorescent.

Claims Text - CLTX (20):

19. The method of lighting according to claim 18, wherein the coolant is selected from the group consisting of ethanol and de-icing fluid Types 1 and 4, and wherein the color is fluorescent.

PGPUB-DOCUMENT-NUMBER: 20030079387

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030079387 A1

TITLE: Display signs and ornaments for holiday seasons

PUBLICATION-DATE: May 1, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Derose, Anthony	Caledon East		CA	

APPL-NO: 09/ 990326

DATE FILED: November 23, 2001

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
CA	2,360,186	2001CA-2,360,186	October 26, 2001

US-CL-CURRENT: 40/544, 362/565 , 362/812

ABSTRACT:

A sign or ornament comprising an etched or otherwise formed translucent light scattering design, lettering, or shape within a matrix contained in the body of a sign or ornament, said sign or ornament having included therewith at least one opening, said opening having contained therewith at least one light source and preferably a light-emitting diode, wherein light emerging from the light source and preferred light-emitting diode incident upon the light scattering translucent design lettering or shape of the sign or the ornament will be enhanced to a much greater extent than any light emanating from the transparent portions of the sign/ornament.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (11):

[0009] U.S. Pat. No. 4,931,227 describes a transparent body having openings therein as seen in FIGS. 5, 6, 8 and 9 wherein a matrix of polymethylmethacrylate is utilized for signs incorporating edge-lighting technology. This particular patent improves edge lighting by utilizing light-reflection material for obtaining a three-dimensional effect. The material has a number of openings or holes extending therethrough formed by placing threads in pre-determined positions while molding the sign, display sheet, or the like, and then pulling the threads through leaving the openings within the material. The threads may be alternatively left in the material when formed having no particularly pre-defined route left to the designer. For the light to provide the most desirable reflection pattern, round openings are recommended. Alternatively, the holes may be coloured using various pigments and dies during the forming process. As described in Example 2 at column 6, line 24, the ornament may be a mobile which is edge-lit. One example is seen in FIGS. 8 and 9 wherein the edge lighting is produced by a **fluorescent** tube to obtain various effects at wave-like openings 2 and 3.

Summary of Invention Paragraph - BSTX (28):

[0025] According to yet another aspect of the invention, there is provided a holiday season ornament comprising a body having provided therein a translucent etched or otherwise formed light scattering surface, ridge or groove, in one embodiment outlining the form of a figure, for example an animal figure, a religious symbol for example a cross, Star of David, crescent moon or the like, an international symbol, stars, or any other well known symbol including Santa Claus, a heart, a candle or the like, wherein said body may be of any desired shape for example, in the shape of a pine cone, a sphere, a hexagonal, a rectangle, a diamond, a pyramid, a cross, an animal shape, for example, a reindeer, a lamb, a camel, or the like, as a flat planar, body or a three dimensional body, said body containing; in a preferred embodiment light scattering elements such as metal shavings, bubbles, or other light scattering elements, and at least one opening for at least one light emitting diode which is positioned so as to light the body with the light exiting from the light emitting diode and being dispersed preferably by said light scattering means, and by said at least one translucent etched or otherwise formed surface, groove or ridge so as to create a dispersion of the light from the body which would remain undispersed had the translucent etched surface, groove, ridge and when present the light scattering means not been provided. In one embodiment for example, the body may be in the shape of a pine cone with the surface of the pine cone shaped body being translucent and being formed or etched so as to simulate the appearance of the rough surface of the perimeter of an actual pine cone. Other fruits may also be similarly presented.

Summary of Invention Paragraph - BSTX (46):

[0043] The invention is not limited by shape, form, colour, or size whatsoever and may take the form by way of example only but not limited to (i) an ornament, for example a Christmas tree string of lights, or individual ornament; (ii) a novelty item, for example a necklace; (iii) a promotional item, for example a display sign for a store window including any alphanumeric character in any language or a internationally recognized symbol or design; (iv) a message, for example an emergency help sign or road marker which may also include any alphanumeric character in any language or a internationally recognized symbol or design; (v) a design, for example a company logo or a clip on personal safety light; (vi) a game, for example a checker or chess board that has sections or playing pieces that illuminate; and (vii) toys of all kinds which may take any possible shape or size in 2 or 3 dimensions.

Detail Description Paragraph - DETX (45):

[0120] 7. Lighted sports logos and mascots on novelty items and collector pieces

Claims Text - CLTX (15):

14. The ornament of claim 12 wherein the secondary light scattering elements are metal shavings, bubbles, or other light scattering elements.

Claims Text - CLTX (44):

43. The design/sign/ornament of claim 1, 8, 12, 21, 27, 29, or 31 further comprising a design selected from the group of designs including patio stones with built in lighting, lighted steps or walkways, posts and stairways, lighted railings and banisters, welcome signs, lighted decorative water fountains for indoors and outdoors, lighted waterfalls, lighted birdbaths, swimming pool accent lighting, lighted driveways and curbs, lighted decorative rock lighting, accent lighting for high-rise buildings, lighted address numbers, lighted signs

for advertising and direction, decorative lighting for building exteriors, lighted perimeter flashing trim elements, accent lighting for doors, windows and frames, lighted baseboards and nightlights, lighted railings, stairs, picture frames, table tops, bar edges, counter tops, door handles and locks, lighted floor tiles, lighted bathroom ceramics, lighted toilet seat, accent lighting for glass partitions with sandblasted images, lighted sports logos and mascots on novelty items and collector pieces, stained glass backlighting (for lighting module with actual stained glass), lighted emergency signs to replace flares for road closures and emergency situations, lighted name plates and trim and license plates for cars and trucks, safety lighting for cyclist, lighted street signs, lighted street names, lighted warning signs, or trouble light (various sizes).

PGPUB-DOCUMENT-NUMBER: 20030066096

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030066096 A1

TITLE: Bioluminescent novelty items

PUBLICATION-DATE: April 3, 2003

US-CL-CURRENT: 800/8, 162/162 , 42/54 , 424/450 , 424/456 , 424/70.14 , 442/131

APPL-NO: 09/ 729133

DATE FILED: December 1, 2000

RELATED-US-APPL-DATA:

child 09729133 A1 20001201

parent continuation-of 09444762 19991122 US PENDING

child 09729133 A1 20001201

parent continuation-of 09135988 19980817 US PATENTED

child 09729133 A1 20001201

parent continuation-in-part-of 08757046 19961125 US PATENTED

child 09729133 A1 20001201

parent continuation-in-part-of 08597274 19960206 US PATENTED

non-provisional-of-provisional 60079624 19980327 US

non-provisional-of-provisional 60089367 19980615 US

RELATED APPLICATIONS

[0001] This applicaiton is a continuation of U.S. application Ser. No. 09/444,762 to Bruce Bryan, filed Nov. 22, 1999, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also continuation of U.S. application Ser. No. 09/135,988 to Bruce Bryan, filed Aug. 17, 1998, now U.S. Pat. No. 6,152,358, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also continuation-in-part of U.S. application Ser. No. 08/757,046 to Bruce Bryan, filed Nov. 25, 1996, now U.S. Pat. No. 5,876,995, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also a continuation-in-part of U.S. application Ser. No. 08/597,274, now allowed, to Bruce Bryan, filed Feb. 6, 1996, entitled "BIOLUMINESCENT NOVELTY ITEMS".

[0002] U.S. application Ser. No. 09/444,762 is a continuation of U.S. application Ser. No. 09/135,988, which is a continuation-in-part of U.S. application Ser. No. 08/757,046, which is a continuation-in-part of U.S. application Ser. No. 08/597,274. The subject matter of each of U.S. application Ser. Nos. 09/135,988, 08/597,274 and 08/757,046 is herein incorporated in its entirety by reference thereto. This application is also

related to provisional application serial numbers 60/079,624 and 60/089,367. The disclosures of each of the above noted patents, applications and provisional applications is incorporated herein by reference thereto.

PGPUB-DOCUMENT-NUMBER: 20030055511

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030055511 A1

TITLE: Shaped particle comprised of bone material and method of making the particle

PUBLICATION-DATE: March 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Schryver, Jeffrey E.	Cordova	TN	US	
Cooper, Michael B.	Memphis	TN	US	
Kinnane, Keith M.	Bartlett	TN	US	
Long, Marc	Memphis	TN	US	
Allen, Trevor	York	TN	GB	
Margerrison, Ed	York	CA	GB	
Morgan, Robert	Bartlett		US	
Bearcroft, Julie A.	York		US	
Harrison, Andrew	Sunnyvale		GB	
Kaiser, William B.			US	

APPL-NO: 10/ 099616

DATE FILED: March 15, 2002

RELATED-US-APPL-DATA:

child 10099616 A1 20020315

parent continuation-in-part-of 09517981 20000303 US PENDING

child 10099616 A1 20020315

parent continuation-in-part-of 09792681 20010223 US PENDING

US-CL-CURRENT: 623/23.5, 623/16.11 , 623/23.63 , 623/919

ABSTRACT:

A shaped particle for use in an array of interlocking particles to repair, replace, improve or augment a bone deficiency is provided. The particle is comprised of bone material and, in a preferred embodiment, has six extremities, and the interstitial spaces between the extremities of one particle accept the extremities of an adjacent particle in an array. In a preferred embodiment, the bone material is demineralized bone material. In some embodiments, the particle is suspended in a material that facilitates application of the particle to bone, and the material may contain biological factors that augment bone growth or prevent infection.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application is a Continuation-in-Part Application of U.S. patent application Ser. No. 09/517,981 filed Mar. 3, 2000 and a Continuation-in-Part Application of U.S. patent application Ser. No. 09/792,681 filed Feb. 23, 2001, both of which are incorporated by reference

herein in their entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (11):
[0095] In a specific embodiment the shaped BGS particle of the present invention is colored to make it more visible. In another specific embodiment differently shaped BGS particles of the present invention are denoted with different colors for better differentiation of the particles. In another specific embodiment, the particles are coated or have contained within them an agent such as green fluorescent protein or blue fluorescent protein to make them fluorescent and therefore more visible.

Detail Description Paragraph - DETX (27):
[0111] The term "JAX.RTM." as used herein is defined as a bone graft substitute particle which generally has the shape of a toy jack. In a specific embodiment, it is a three-dimensional six-armed star-like shape.

Detail Description Paragraph - DETX (62):
[0143] In a preferred embodiment the shaped particle of polymer has as the ends of its extremities a bubble shape which may provide a "snap-fit" for adjacent interlocking polymeric shaped particles, such as the particles illustrated in FIGS. 4 and 5.

US-PAT-NO: 6649357

DOCUMENT-IDENTIFIER: US 6649357 B2

TITLE: Apparatus and method for detecting and identifying infectious agents

DATE-ISSUED: November 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bryan; Bruce J.	Beverly Hills	CA	N/A	N/A
Gaalema; Stephen	Colorado Springs	CO	N/A	N/A
Murphy; Randall B.	Irvington	NY	N/A	N/A

APPL-NO: 10/ 126798

DATE FILED: April 19, 2002

PARENT-CASE:

RELATED APPLICATIONS

This application is a divisional of application Ser. No. 08/990,103 filed Dec. 12, 1997 now U.S. Pat. No. 6,458,547. This application claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional application Serial No. 60/037,675, filed Feb. 11, 1997 and to U.S. Provisional application Serial No. 60/033,745, filed Dec. 12, 1996.

Certain subject matter in this application is related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS" (B), and to U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES" and to U.S. Provisional application Serial No. 60/023,374, filed Aug. 8, 1996, entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES", and also to published International PCT application No. WO _____.

The subject matter of each of the above noted U.S. applications, provisional applications and international application is herein incorporated by reference in its entirety.

US-CL-CURRENT: 435/7.1, 356/215 , 356/222 , 356/317 , 422/57 , 422/58 , 422/68.1 , 422/82.05 , 422/82.08 , 435/288.7 , 435/6 , 435/7.9 , 435/808 , 435/973 , 435/975 , 436/164 , 436/172 , 436/518 , 436/524 , 436/527 , 436/532 , 436/805

ABSTRACT:

Solid phase methods for the identification of an analyte in a biological medium, such as a body fluid, using bioluminescence are provided. A chip designed for performing the method and detecting the bioluminescence is also provided. Methods employing biomineralization for depositing silicon on a matrix support are also provided. A synthetic synapse is also provided.

12 Claims, 24 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 19

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Parent Case Text - PCTX (3):
Certain subject matter in this application is related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS" (B), and to U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES" and to U.S. Provisional application Serial No. 60/023,374, filed Aug. 8, 1996, entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES", and also to published International PCT application No. WO _____.

Brief Summary Text - BSTX (5):
Luminescence is a phenomenon in which energy is specifically channeled to a molecule to produce an excited state. Return to a lower energy state is accompanied by release of a photon (hy). Luminescence includes fluorescence, phosphorescence, chemiluminescence and bioluminescence. Bioluminescence is the process by which living organisms emit light that is visible to other organisms. Luminescence may be represented as follows:

Detailed Description Text - DETX (1):
DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS TABLE OF CONTENTS A. Definitions B. Bioluminescence generating systems 1. General description a. Luciferases b. Luciferins c. Activators d. Reactions 2. Ctenophore and coelenterate systems a. The aequorin system (1) Aequorin photoprotein (2) Luciferin b. The Renilla system 3. Crustacean, particular Cyrpidina [Vargula], systems a. Vargula Luciferase (1) Purification from Cypridina (2) Preparation by Recombinant Methods b. Vargula luciferin c. Reaction 4. Insect bioluminescence generating systems including fireflies, click beetles, and other insect systems a. Luciferase b. Luciferin c. Reaction 5. Bacterial systems a. Luciferases b. Luciferins c. Reactions 6. Other systems a. Dinoflagellate bioluminescence generating systems b. Systems from Mmlluscs, such as Latia and Pholas c. Earthworms and other annelids d. Glow worms e. Marine polycheate worm systems f. South American railway beetle 7. Fluorescent Proteins a. Green and blue fluorescent proteins b. Phycobiliproteins

Detailed Description Text - DETX (38):
As used herein, a substrate refers to any matrix that is used either directly or following suitable derivatization, as a solid support for chemical synthesis, assays and other such processes. Preferred substrates herein, are silicon substrates or siliconized substrates that are derivatized on the surface intended for linkage of anti-ligands and ligands and other macromolecules, including the fluorescent proteins, phycobiliproteins and other emission shifters.

Detailed Description Text - DETX (74):

The aequorin system is well known [see, e.g., Tsuji et al. (1986) "Site-specific mutagenesis of the calcium-binding photoprotein aequorin," Proc. Natl. Acad. Sci. USA 83:8107-8111; Prasher et al. (1985) "Cloning and Expression of the cDNA Coding for Aequorin, a Bioluminescent Calcium-Binding Protein," Biochemical and Biophysical Research Communications 126:1259-1268; Prasher et al. (1986) Methods in Enzymology 133:288-297; Prasher, et al. (1987) "Sequence Comparisons of cDNAs Encoding for Aequorin Isotypes," Biochemistry 26:1326-1332; Charbonneau et al. (1985) "Amino Acid Sequence of the Calcium-Dependent Photoprotein Aequorin," Biochemistry 24:6762-6771; Shimomura et al. (1981) "Resistivity to denaturation of the apoprotein of aequorin and reconstitution of the luminescent photoprotein from the partially denatured apoprotein," Biochem. J. 199:825-828; Inouye et al. (1989) J. Biochem. 105:473-477; Inouye et al. (1986) "Expression of Apoaequorin Complementary DNA in Escherichia coli," Biochemistry 25:8425-8429; Inouye et al. (1985) "Cloning and sequence analysis of cDNA for the luminescent protein aequorin," Proc. Natl. Acad. Sci. USA 82:3154-3158; Prendergast, et al. (1978) "Chemical and Physical Properties of Aequorin and the Green Fluorescent Protein Isolated from Aequorea forskalea" J. Am. Chem. Soc. 17:3448-3453; European Patent Application 0 540 064 A1; European Patent Application 0 226 979 A2, European Patent Application 0 245 093 A1 and European Patent Specification 0 245 093 B1; U.S. Pat. No. 5,093,240; U.S. Pat. No. 5,360,728; U.S. Pat. No. 5,139,937; U.S. Pat. No. 5,422,266; U.S. Pat. No. 5,023,181; U.S. Pat. No. 5,162,227; and SEQ ID Nos. 5-13, which set forth DNA encoding the apoprotein; and a form, described in U.S. Pat. No. 5,162,227, European Patent Application 0 540 064 A1 and Sealite Sciences Technical Report No. 3 (1994), is commercially available from Sealite, Sciences, Bogart, Ga. as AQUALITE.RTM.].

Detailed Description Text - DETX (158):
DNA encoding luciferase from the fluorescent bacterium Alteromonas hanedai is known [CHISSO CORP; see, also, Japanese application JP 7222590, published Aug. 22, 1995]. The reduced flavin mononucleotide [FMNH.sub.2 ; luciferin] reacts with oxygen in the presence of bacterial luciferase to produce an intermediate peroxy flavin. This intermediate reacts with a long-chain aldehyde [tetradecanal] to form the acid and the luciferase-bound hydroxy flavin in its excited state. The excited luciferase-bound hydroxy flavin then emits light and dissociates from the luciferase as the oxidized flavin mononucleotide [FMN] and water. In vivo FMN is reduced again and recycled, and the aldehyde is regenerated from the acid.

Detailed Description Text - DETX (182):
7. Fluorescent Proteins

Detailed Description Text - DETX (183):
a. Green and Blue Fluorescent Proteins

Detailed Description Text - DETX (184):
As described herein, blue light is produced using the Renilla luciferase or the Aequorea photoprotein in the presence of Ca.sup.2+ and the coelenterazine luciferin or analog thereof. This light can be converted into a green light if a green fluorescent protein (GFP) is added to the reaction. Green fluorescent proteins, which have been purified [see, e.g., Prasher et al. (1992) Gene 111:229-233] and also cloned [see, e.g., International PCT Application No. WO 95/07463, which is based on U.S. application Ser. No. 08/119,678 and U.S. application Ser. No. 08/192,274, which are herein incorporated by reference], are used by cnidarians as energy-transfer acceptors. GFPs fluoresce in vivo

upon receiving energy from a luciferase-oxyluciferein excited-state complex or a Ca.sup.2+ -activated photoprotein. The chromophore is modified amino acid residues within the polypeptide. The best characterized GFPs are those of Aequorea and Renilla [see, e.g., Prasher et al. (1992) Gene 111:229-233; Hart, et al. (1979) Biochemistry 18:2204-2210]. For example, a green fluorescent protein [GFP] from Aequorea victoria contains 238 amino acids, absorbs blue light and emits green light. Thus, inclusion of this protein in a composition containing the aequorin photoprotein charged with coelenterazine and oxygen, can, in the presence of calcium, result in the production of green light. Thus, it is contemplated that GFPs may be included in the bioluminescence generating reactions that employ the aequorin or Renilla luciferases or other suitable luciferase in order to enhance or alter color of the resulting bioluminescence.

Detailed Description Text - DETX (185):

GFPs are activated by blue light to emit green light and thus may be used in the absence of luciferase and in conjunction with an external light source with novelty items, as described herein. Similarly, blue fluorescent proteins (BFPs), such as from Vibrio fischeri, Vibrio harveyi or Photobacterium phosphoreum, may be used in conjunction with an external light source of appropriate wavelength to generate blue light. (See for example, Karatani, et al., "A blue fluorescent protein from a yellow-emitting luminous bacterium," Photochem. Photobiol. 55(2):293-299 (1992); Lee, et al., "Purification of a blue-fluorescent protein from the bioluminescent bacterium Photobacterium phosphoreum" Methods Enzymol. (Biolumin. Chemilumin.) 57:226-234 (1978); and Gast, et al. "Separation of a blue fluorescence protein from bacterial luciferase" Biochem. Biophys. Res. Commun. 80(1):14-21 (1978), each, as all references cited herein, incorporated in its entirety by reference herein.) In particular, GFPs, and/or BFPs or other such fluorescent proteins may be used in the methods provided herein for the detection of infectious agents by binding an analyte to one or more anti ligand-GFP conjugate(s) at a plurality of locations and illuminating the chip with light of an appropriate wavelength to cause the fluorescent proteins to fluoresce whereby the emitted fluorescence is detected by the photodiodoes in the chip.

Detailed Description Text - DETX (186):

GFPs and/or BFPs or other such fluorescent proteins may be used in conjunction with any of the chips or devices described herein. These fluorescent proteins may also be used alone or in combination with bioluminescence generating systems to produce an array of colors. They may be used in combinations such that the color, for example, of the emitted light may be altered to maximize the amount of light available for detection by the photodiodes of the chip.

Detailed Description Text - DETX (188):

Phycobiliproteins are water soluble fluorescent proteins derived from cyanobacteria and eukaryotic algae [see, e.g., Apt et al. (1995) J. Mol. Biol. 238:79-96; Glazer (1982) Ann. Rev. Microbiol. 36:173-198; and Fairchild et al. (1994) J. of Biol. Chem. 269:8686-8694]. These proteins have been used as fluroescent labels in immmunoassay [see, Kronick (1986) J. of Immunolog. Meth. 92:1-13], the proteins have been isolated and DNA encoding them is also available [see, e.g., Pilot et al. (1984) Proc. Natl. Acad. Sci. U.S.A. 81:6983-6987; Lui et al. (1993) Plant Physiol 103:293-294; and Houmard et al. (1988) J. Bacteriol. 170:5512-5521; the proteins are commercially available from, for example, ProZyme, Inc., San Leandro, Calif.].

Detailed Description Text - DETX (189):
In these organisms, the phycobiliproteins are arranged in subcellular structures termed phycobilisomes and function as accessory pigments that participate in photosynthetic reactions by absorbing visible light and transferring the derived energy to chlorophyll via a direct fluorescence energy transfer mechanism.

Detailed Description Text - DETX (192):
As described above for GFPs & BFPs, phycobiliproteins are also activated by visible light of the appropriate wavelength and thus may be used in the absence of luciferase and in conjunction with an external light source to illuminate the phycobiliprotein bound to the chip at locations where analyte has been detected. In particular, phycobiliproteins may be covalently bound to one or more anti-ligand specific for the targeted analyte and illuminated with light of an appropriate wavelength to cause the fluorescent proteins to fluoresce and the fluorescence is measured by the photodiodes of the chip at that location of the array. The data signals are sent to the computer processor and analyzed. As noted above, these proteins may be used in combination with other fluoresent proteins and/or bioluminescence generating systems to produce an array of colors or to provide different colors over time that can be detected by the photodiodes of the chip.

Detailed Description Text - DETX (275):
The efficiency of the derivatization of the surface of the chip may be determined by coupling an appropriate fluorescent amine (carboxyl derivatized) or fluorescent carboxylic acid (amino derivatized) to the surface of the chip by exciting the fluorescence of the bound molecules using a laser of appropriate wavelength. Appropriate compounds for this purpose may be amino, carboxyl or other reactive derivatives of fluorescein, rhodamine or Texas Red, which are known to those of skill in the art and are also commercially available (e.g., see Molecular Probes, Inc.).

Detailed Description Text - DETX (276):
The isothiocyanates of fluorescein, rhodamine, or Texas Red, for example, react in an irreversible and covalent manner with any free amino groups on the silica surface. A solution of an effective concentration of fluorescein (about 10 mM) isothiocyanate (mixed isomers) in acetone or dioxane is placed on the amine-derivatized silica of the chip for sufficient time, typically about 30 minutes at ambient temperatures. To remove all unreacted material, the chip is washed with hot (i.e., 60.degree. C.) solutions of acetone, hexane and pentane or other suitable solvent. A region on the same chip that has not been chemically derivatized is similarly treated with the fluorescein isothiocyanate as a control. A small amount of direct covalent reaction with the glass is possible and thus the control should be performed to indicate background levels. The fluorescence of the bound fluorescein can be excited using a suitable sources, such as an argon ion laser (e.g., 488 nm), preferably using a 45-degree angle geometry. The argon laser can further contain a photomultiplier equipped with a 10 nm bandpass filter for detecting the emitted fluorescence signal at about 520 nm. The amount of fluorescence detected is a function of the extent and efficiency of derivatization.

Detailed Description Text - DETX (321):
Alternatively, the acetylcholine binding region of acetylcholine esterase may be fused to a fluorochrome or phycobiliprotein and used in conjunction with

a laser. In this embodiment, monochromatic light of a known wavelength is generated by a laser to excite the fluorophore and the emitted fluorescence is directed to the photodiode surface of the chip by a parabolic mirror [see e.g., FIGS. 17 & 18], and the emitted light detected and employed as described for the bioluminescence.

Detailed Description Text - DETX (322):
FIG. 17 shows a silicon synapse to provide neuronal input to interface with a computer for the purpose of bypassing spinal cord lesions so limited motor control can be brought to muscles distal to the spinal lesion. FIG. 18 shows a detail view of acetylcholinesterase-fluorescent fusion protein. For the neuronal axon to transmit a signal to the silicon synapse the nerve must release acetylcholine in the usual manner. The acetylcholine must be in close proximity to the fusion protein. Keeping the neuron associated may be produced by release of growth hormones slowly into the area via a microport. Also, an electrode is nearby also causing the neuron to "feel" the artificial synapse, by the input of weak+small electric currents. There are two versions of this synapse, one "crude" that does not have a laser, only a CCD and a luciferin port. The "elegant" uses a laser to excite the fusion protein to fluoresce if acetylcholine is present or the converse. The specifics of the fusion protein are: (1) conformational change to become active when ACH is present, (2) non-antigenic, (3) stable protein so it does not have to be changed. FIG. 19 shows the placement of silicon synapse electrodes. Placement of the electrodes into the correct stereotaxic locations can be achieved by MRI localization. Laser microholes can be drilled into the spinal cord with suitable CO.sub.2 or other laser. Placement would be from superficial to deep along the known pathways and there could be several wires leading to the computer. RT/LT/LAT to MED/VENT to Dorsal at first 2 channels on each side but many more could be placed. Muscle movements could be initiated by insertion of permanent electrodes into various muscle bundles. The patient will control the output by thinking about it and thereby relearning motor skills, such as walking.

Claims Text - CLTX (8):
8. The method of claim 1, wherein the bioluminescence generating system further comprises a fluorescent protein.

Claims Text - CLTX (9):
9. The method of claim 8, wherein the fluorescent protein is selected from the group consisting of green fluorescent protein (GFP), blue fluorescent protein (BFP) and a phycobiliprotein.

Other Reference Publication - OREF (32):
Certified Translation of European Patent 0 246 174, Process for obtaining a fluorescent effect and products obtained by means of this process.

Other Reference Publication - OREF (45):
Database Derwent #76-7624X/197641 (citing French Patent 2292595, Bubble fountain with means generating pulsating air--and diffusing odour of liq. by bursting of bubbles.

Other Reference Publication - OREF (67):
Gast et al., Separation of a blue fluorescence protein from bacterial luciferase. Biochem. Biophys. Res. Commun. 80(1): 14-21 (1978).

Other Reference Publication - OREF (74):
Hart et al. "Renilla reniformis bioluminescence: Luciferase-catalyzed production of nonradiating excited states from luciferin analogues and elucidation of the excited state species involoved in energy transfer to Renilla green fluorescent protein", (1979) Biochemistry 18:2204-2210 (1979).

Other Reference Publication - OREF (95):
Karatani et al., A blue fluorescent protein from a yellow-emitting luminous bacterium, Photochem. Photobiol. 55(2): 293-299 (1992).

Other Reference Publication - OREF (104):
Kronick, The use of phycobiliproteins as fluorescent labels in immunoassay, J. Immunolog. Meth. 92: 1-13 (1986).

Other Reference Publication - OREF (107):
Lee et al., "Purification of a blue-fluorescent protein from the bioluminescent bacterium photobacterium phosphoreum," Methods Enzymol. (Biolumin. Chemilumin.), 57:226-234 (1978).

Other Reference Publication - OREF (139):
Peterson, I., Glimpses inside a tiny, flashing bubble, Science News 150:214, (1996).

Other Reference Publication - OREF (148):
Prasher et al., Primary structure of the Aequorea victoria green-fluorescent protein, Gene 111:229-233 (1992).

Other Reference Publication - OREF (151):
Prendergast et al., Chemical and physical properties of aequorin and the green fluorescent protein isolated from Aequorea forsk.ang.lea, Biochemistry 17: 3448-53 (1978).

Other Reference Publication - OREF (164):
Smalley et al., "Localization of fluorescent compounds in the firefly light organ", J. Histochem. Cytochem. 28(4):323-329 (1980).

Other Reference Publication - OREF (206):
Chalfie, Green fluorescent protein, Photochemistry and Photobiology, 62(4):651-656 (1995).

Other Reference Publication - OREF (208):
Delagrave et al., Red-shifted excitation mutants of the green fluorescent protein, Bio/Technology 13(2):151-154 (1995).

Other Reference Publication - OREF (209):
Ehrig et al., Green-fluorescent protein mutants with altered fluorence excitationspectra, FEBS Letters 267:163-166 (1995).

Other Reference Publication - OREF (210):
Fratamico et al., Construction and characterization of Escherichia coli 0157:H7 strains expressing firefly luciferase and green fluorescent protein and their use in survival studies, J of Food Protection 60(10):1167-1173 (1997).

Other Reference Publication - OREF (211):
Heim et al., Engineering green fluorescent protein for improved brightness, longer wavelengths and fluorescence resonance energy transfer, Current Biology 6(2):178-182 (1996).

Other Reference Publication - OREF (212):
Mitra et al., Fluorescence resonance energy tranfer between blue-emitting and red-shifted excitation derivatives of the green fluorescent protein, Gene 73(1):13-17 (1996).

Other Reference Publication - OREF (213):
Romoser et al., Detection in living cells of Ca2+-dependent changes in the fluorescence emission of an indicator composed of two green fluorescent protein variants liked by a calmodulin-binding sequence, J. of Biolog. Chem. 272(20):13270-13274 (1997).

US-PAT-NO: 6649356

DOCUMENT-IDENTIFIER: US 6649356 B2

TITLE: Apparatus and method for detecting and identifying infectious agents

DATE-ISSUED: November 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bryan; Bruce J.	Beverly Hills	CA	N/A	N/A
Gaalema; Stephen	Colorado Springs	CO	N/A	N/A
Murphy; Randall B.	Irvington	NY	N/A	N/A

APPL-NO: 10/ 126139

DATE FILED: April 19, 2002

PARENT-CASE:

RELATED APPLICATIONS

This application is a divisional of application Ser. No. 08/990,103 filed Dec. 12, 1997 now U.S. Pat. No. 6,458,547.This application claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional application Serial No. 60/037,675, filed Feb. 11, 1997 and to U.S. Provisional application Serial No. 60/033,745, filed Dec. 12, 1996.

Certain subject matter in this application is related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS" (B), and to U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES" and to U.S. Provisional application Ser. No. 60/023,374, filed Aug. 8, 1996, entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES", and also to published International PCT application No. WO 97/29,319.

The subject matter of each of the above noted U.S. applications, provisional applications and International application is herein incorporated by reference in its entirety.

US-CL-CURRENT: 435/7.1, 356/215 , 356/222 , 356/317 , 422/57 , 422/58 , 422/68.1 , 422/82.05 , 422/82.08 , 435/288.7 , 435/6 , 435/7.9 , 435/808 , 435/973 , 435/975 , 436/122 , 436/164 , 436/518 , 436/524 , 436/527 , 436/532 , 436/805

ABSTRACT:

Solid phase methods for the identification of an analyte in a biological medium, such as a body fluid, using bioluminescence are provided. A chip designed for performing the method and detecting the bioluminescence is also provided. Methods employing biomineralization for depositing silicon on a matrix support are also provided. A synthetic synapse is also provided.

7 Claims, 24 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 19

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Parent Case Text - PCTX (3):
Certain subject matter in this application is related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS" (B), and to U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES" and to U.S. Provisional application Ser. No. 60/023,374, filed Aug. 8, 1996, entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES", and also to published International PCT application No. WO 97/29,319.

Brief Summary Text - BSTX (5):
Luminescence is a phenomenon in which energy is specifically channeled to a molecule to produce an excited state. Return to a lower energy state is accompanied by release of a photon (h.gamma.). Luminescence includes fluorescence, phosphorescence, chemiluminescence and bioluminescence. Bioluminescence is the process by which living organisms emit light that is visible to other organisms. Luminescence may be represented as follows:

Detailed Description Text - DETX (2):
Table of Contents A. Definitions B. Bioluminescence generating systems 1. General description a. Luciferases b. Luciferins c. Activators d. Reactions 2. Ctenophore and coelenterate systems a. The aequorin system (1) Aequorin photoprotein (2) Luciferin b. The Renilla system 3. Crustacean, particular Cyrpidina [Vargula], systems a. Vargula luciferase (1) Purification from Cypridina (2) Preparation by Recombinant Methods b. Vargula luciferin c. Reaction 4. Insect bioluminescence generating systems including fireflies, click beetles, and other insect systems a. Luciferase b. Luciferin c. Reaction 5. Bacterial systems a. Luciferases b. Luciferins c. Reactions 6. Other systems a. Dinoflagellate bioluminescence generating systems b. Systems from molluscs, such as Latia and Pholas c. Earthworms and other annelids d. Glow worms e. Marine polycheate worm systems f. South American railway beetle 7. Fluorescent proteins a. Green and blue fluorescent proteins b. Phycobiliproteins C. Design and Fabrication of Chips 1. Nonself-addressable chips 2. Self-addressable chips a. Matrix materials b. Fabrication procedures i. Microlithography ii. Micromachining c. Self addressing of chips 3. Attachment of biological molecules to chips a. Derivatization of silica substrates b. Attachment of biological molecules D. Formation of luciferase conjugates 1. Linkers 2. Luciferase fusion proteins 3. Nucleic acid and peptide nucleic acid conjugates E. Radiolarians and diatoms for deposition of silicon on matrices F. Methods employing the chip A. Definitions

Detailed Description Text - DETX (37):
As used herein, a substrate refers to any matrix that is used either directly or following suitable derivatization, as a solid support for chemical synthesis, assays and other such processes. Preferred substrates herein, are

silicon substrates or siliconized substrates that are derivatized on the surface intended for linkage of anti-ligands and ligands and other macromolecules, including the fluorescent proteins, phycobiliproteins and other emission shifters.

Detailed Description Text - DETX (65):
The aequorin system is well known [see, e.g., Tsuji et al. (1986) "Site-specific mutagenesis of the calcium-binding photoprotein aequorin," Proc. Natl. Acad. Sci. USA 83:8107-8111; Prasher et al. (1985) "Cloning and Expression of the cDNA Coding for Aequorin, a Bioluminescent Calcium-Binding Protein," Biochemical and Biophysical Research Communications 126:1259-1268; Prasher et al. (1986) Methods in Enzymology 133:288-297; Prasher, et al. (1987) "Sequence Comparisons of cDNAs Encoding for Aequorin Isotypes," Biochemistry 26:1326-1332; Charbonneau et al. (1985) "Amino Acid Sequence of the Calcium-Dependent Photoprotein Aequorin," Biochemistry 24:6762-6771; Shimomura et al. (1981) "Resistivity to denaturation of the apoprotein of aequorin and reconstitution of the luminescent photoprotein from the partially denatured apoprotein," Biochem. J. 199:825-828; Inouye et al. (1989) J. Biochem. 105:473-477; Inouye et al. (1986) "Expression of Apoaequorin Complementary DNA in Escherichia coli," Biochemistry 25:8425-8429; Inouye et al. (1985) "Cloning and sequence analysis of cDNA for the luminescent protein aequorin," Proc. Natl. Acad. Sci. USA 82:3154-3158; Prendergast, et al. (1978) "Chemical and Physical Properties of Aequorin and the Green Fluorescent Protein Isolated from Aequorea forskalea" J. Am. Chem. Soc. 17:3448-3453; European Patent Application 0 540 064 A1; European Patent Application 0 226 979 A2, European Patent Application 0 245 093 A1 and European Patent Specification 0 245 093 B1; U.S. Pat. Nos. 5,093,240; 5,360,728; 5,139,937; 5,422,266; 5,023,181; 5,162,227; and SEQ ID Nos. 5-13, which set forth DNA encoding the apoprotein; and a form, described in U.S. Pat. No. 5,162,227, European Patent Application 0 540 064 A1 and Sealite Sciences Technical Report No. 3 (1994), is commercially available from Sealite, Sciences, Bogart, Ga. as AQUALITE.RTM.].

Detailed Description Text - DETX (132):
DNA encoding luciferase from the fluorescent bacterium Alteromonas hanedai is known [CHISSO CORP; see, also, Japanese application JP 7222590, published Aug. 22, 1995]. The reduced flavin mononucleotide [FMNH.sub.2 ; luciferin] reacts with oxygen in the presence of bacterial luciferase to produce an intermediate peroxy flavin. This intermediate reacts with a long-chain aldehyde [tetradecanal] to form the acid and the luciferase-bound hydroxy flavin in its excited state. The excited luciferase-bound hydroxy flavin then emits light and dissociates from the luciferase as the oxidized flavin mononucleotide [FMN] and water. In vivo FMN is reduced again and recycled, and the aldehyde is regenerated from the acid.

Detailed Description Text - DETX (147):
Of interest herein, are luciferases and bioluminescence generating systems that generate red light. These include luciferases found in species of Aristostomias, such as A. scintillans [see, e.g., O'Day et al. (1974) Vision Res. 14:545-550], Pachystomias, Malacosteus, such as M. niger. 7. Fluorescent Proteins a. Green and blue fluorescent proteins

Detailed Description Text - DETX (148):
As described herein, blue light is produced using the Renilla luciferase or the Aequorea photoprotein in the presence of Ca.sup.2+ and the coelenterazine luciferin or analog thereof. This light can be converted into a green light if

a green fluorescent protein (GFP) is added to the reaction. Green fluorescent proteins, which have been purified [see, e.g., Prasher et al. (1992) Gene 111:229-233] and also cloned [see, e.g., International PCT Application No. WO 95/07463, which is based on U.S. application Ser. No. 08/119,678 and U.S. application Ser. No. 08/192,274, which are herein incorporated by reference], are used by cnidarians as energy-transfer acceptors. GFPs fluoresce in vivo upon receiving energy from a luciferase-oxyluciferein excited-state complex or a Ca.sup.2+ -activated photoprotein. The chromophore is modified amino acid residues within the polypeptide. The best characterized GFPs are those of Aequorea and Renilla [see, e.g., Prasher et al. (1992) Gene 111:229-233; Hart, et al. (1979)Biochemistry 18:2204-2210]. For example, a green fluorescent protein [GFP] from Aequorea victoria contains 238 amino acids, absorbs blue light and emits green light. Thus, inclusion of this protein in a composition containing the aequorin photoprotein charged with coelenterazine and oxygen, can, in the presence of calcium, result in the production of green light. Thus, it is contemplated that GFPs may be included in the bioluminescence generating reactions that employ the aequorin or Renilla luciferases or other suitable luciferase in order to enhance or alter color of the resulting bioluminescence.

Detailed Description Text - DETX (149):

GFPs are activated by blue light to emit green light and thus may be used in the absence of luciferase and in conjunction with an external light source with novelty items, as described herein. Similarly, blue fluorescent proteins (BFPs), such as from Vibrio fischeri, Vibrio harveyi or Photobacterium phosphoreum, may be used in conjunction with an external light source of appropriate wavelength to generate blue light. (See for example, Karatani, et al., "A blue fluorescent protein from a yellow-emitting luminous bacterium," Photochem. Photobiol. 55(2):293-299 (1992); Lee, et al., "Purification of a blue-fluorescent protein from the bioluminescent bacterium Photobacterium phosphoreum" Methods Enzymol. (Biolumin. Chemilumin.) 57:226-234 (1978); and Gast, et al. "Separation of a blue fluorescence protein from bacterial luciferase" Biochem. Biophys. Res. Commun. 80(1):14-21 (1978), each, as all references cited herein, incorporated in its entirety by reference herein.) In particular, GFPs, and/or BFPs or other such fluorescent proteins may be used in the methods provided herein for the detection of infectious agents by binding an analyte to one or more anti ligand-GFP conjugate(s) at a plurality of locations and illuminating the chip with light of an appropriate wavelength to cause the fluorescent proteins to fluoresce whereby the emitted fluorescence is detected by the photodiodoes in the chip.

Detailed Description Text - DETX (150):

GFPs and/or BFPs or other such fluorescent proteins may be used in conjunction with any of the chips or devices described herein. These fluorescent proteins may also be used alone or in combination with bioluminescence generating systems to produce an array of colors. They may be used in combinations such that the color, for example, of the emitted light may be altered to maximize the amount of light available for detection by the photodiodes of the chip. b. Phycobiliproteins

Detailed Description Text - DETX (151):

Phycobiliproteins are water soluble fluorescent proteins derived from cyanobacteria and eukaryotic algae [see, e.g., Apt et al. (1995) J. Mol. Biol. 238:79-96; Glazer (1982) Ann. Rev. Microbiol. 36:173-198; and Fairchild et al (1994) J. of Biol. Chem. 269:8686-8694]. These proteins have been used as fluroescent labels in immmunoassay [see, Kronick (1986) J. of Immunolog. Meth.

92:1-13], the proteins have been isolated and DNA encoding them is also available [see, e.g., Pilot et al. (1984) Proc. Natl. Acad. Sci. U.S.A. 81:6983-6987; Lui et al. (1993) Plant Physiol 103:293-294; and Houmard et al. (1988) J. Bacteriol. 170:5512-5521; the proteins are commercially available from, for example, ProZyme, Inc., San Leandro, Calif.].

Detailed Description Text - DETX (152):
In these organisms, the phycobiliproteins are arranged in subcellular structures termed phycobilisomes and function as accessory pigments that participate in photosynthetic reactions by absorbing visible light and transferring the derived energy to chlorophyll via a direct fluorescence energy transfer mechanism.

Detailed Description Text - DETX (155):
As described above for GFPs & BFPs, phycobiliproteins are also activated by visible light of the appropriate wavelength and thus may be used in the absence of luciferase and in conjunction with an external light source to illuminate the phycobiliprotein bound to the chip at locations where analyte has been detected. In particular, phycobiliproteins may be covalently bound to one or more anti-ligand specific for the targeted analyte and illuminated with light of an appropriate wavelength to cause the fluorescent proteins to fluoresce and the fluorescence is measured by the photodiodes of the chip at that location of the array. The data signals are sent to the computer processor and analyzed. As noted above, these proteins may be used in combination with other fluoresent proteins and/or bioluminescence generating systems to produce an array of colors or to provide different colors over time that can be detected by the photodiodes of the chip.

Detailed Description Text - DETX (227):
The efficiency of the derivatization of the surface of the chip may be determined by coupling an appropriate fluorescent amine (carboxyl derivatized) or fluorescent carboxylic acid (amino derivatized) to the surface of the chip by exciting the fluorescence of the bound molecules using a laser of appropriate wavelength. Appropriate compounds for this purpose may be amino, carboxyl or other reactive derivatives of fluorescein, rhodamine or Texas Red, which are known to those of skill in the art and are also commercially available (e.g., see Molecular Probes, Inc.).

Detailed Description Text - DETX (228):
The isothiocyanates of fluorescein, rhodamine, or Texas Red, for example, react in an irreversible and covalent manner with any free amino groups on the silica surface. A solution of an effective concentration of fluorescein (about 10 mM) isothiocyanate (mixed isomers) in acetone or dioxane is placed on the amine-derivatized silica of the chip for sufficient time, typically about 30 minutes at ambient temperatures. To remove all unreacted material, the chip is washed with hot (i.e., 60.degree. C.) solutions of acetone, hexane and pentane or other suitable solvent. A region on the same chip that has not been chemically derivatized is similarly treated with the fluorescein isothiocyanate as a control. A small amount of direct covalent reaction with the glass is possible and thus the control should be performed to indicate background levels. The fluorescence of the bound fluorescein can be excited using a suitable sources, such as an argon ion laser (e.g., 488 nm), preferably using a 45-degree angle geometry. The argon laser can further contain a photomultiplier equipped with a 10 nm bandpass filter for detecting the emitted fluorescence signal at about 520 nm. The amount of fluorescence detected is a

function of the extent and efficiency of derivatization.

Detailed Description Text - DETX (263):
Alternatively, the acetylcholine binding region of acetylcholine esterase may be fused to a fluorochrome or phycobiliprotein and used in conjunction with a laser. In this embodiment, monochromatic light of a known wavelength is generated by a laser to excite the fluorophore and the emitted fluorescence is directed to the photodiode surface of the chip by a parabolic mirror [see e.g., FIGS. 17 & 18], and the emitted light detected and employed as described for the bioluminescence.

Claims Text - CLTX (6):
6. The kit of claim 1, further comprising a composition comprising a fluorescent protein.

Claims Text - CLTX (7):
7. The kit of claim 6, wherein the fluorescent protein is selected from the group consisting of green fluorescent protein (GFP), blue fluorescent protein (BFP) and a phycobiliprotein.

Other Reference Publication - OREF (32):
Certified Translation of European Patent 0 246 174, Process for obtaining a fluorescent effect and products obtained by means of this process.

Other Reference Publication - OREF (45):
Database Derwent #76-76247X/197641 (citing French Patent 2292595, Bubble fountain with means generating pulsating air--and diffusing odour of liq. by bursting of bubbles.

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Other Reference Publication - OREF (74):
Hart et al. "Renilla reniformis bioluminescence: Luciferase-catalyzed production of nonradiating excited states from luciferin analogues and elucidation of the excited state species involved in energy transfer to Renilla green fluorescent protein", (1979) Biochemistry 18:2204-2110 (1979).

Other Reference Publication - OREF (95):
Karatani et al. A blue fluorescent protein from a yellow-emitting luminous bacterium, Photochem. Photobiol. 55(2): 293-299 (1992).

Other Reference Publication - OREF (104):
Kronick, The use of phycobiliproteins as fluorescent labels in immunoassay, J. Immunolog. Meth. 92: 1-13 (1986).

Other Reference Publication - OREF (107):
Lee et al., "Purification of a blue-fluorescent protein from the

bioluminescent bacterium pPhotobacterium hosphoreum," Methods Enzymol. (Biolumin. Chemilumin.), 57:226-234 (1978).

Other Reference Publication - OREF (139):
Peterson, I., Glimpses inside a tiny, flashing bubble, Science News 150:214, (1996).

Other Reference Publication - OREF (148):
Prasher et al., Primary structure of the Aequorea victoria green-fluorescent protein, Gene 111:229-233 (1992).

Other Reference Publication - OREF (151):
Prendergast et al., Chemical and physical porperties of aequorin and the green fluorescent protein isolated from Aequorea forsk.ang.lea, Biochemistry 17: 3448-53 (1978).

Other Reference Publication - OREF (164):
Smalley et al., "Localization of fluorescent compounds in the firefly light organ", J. Histochem. Cytochem. 28(4):323-329 (1980).

Other Reference Publication - OREF (206):
Chalfie, Green fluorescent protein, Photochemistry and Photobiology, 62(4):651-656 (1995).

Other Reference Publication - OREF (208):
Delagrave et al., Red-shifted excitation mutants of the green fluorescent protein, Bio/Technology 13(2):151-154 (1995).

Other Reference Publication - OREF (209):
Ehrig et al., Green-fluorescent protein mutants with altered fluorence excitationspectra, FEBS Letters 367:163-166 (1995).

Other Reference Publication - OREF (210):
Fratamico et al., Construction and characterization of Escherichia coli 0157:H7 strains expressing firefly luciferase and green fluorescent protein and their use in survival studies, J of Food Protection 60(10):1167-1173 (1997).

Other Reference Publication - OREF (211):
Heim et al., Engineering green flourescent protein for improved brightness, longer wavelengths and fluorescence resonance energy transfer, Current Biology 6(2):178-182 (1996).

Other Reference Publication - OREF (212):
Mitra et al., Fluorescence resonance energy transfer between blue-emitting and red-shifted excitation derivatives of the green fluorescent protein, Gene 73(1):13-17 (1996).

Other Reference Publication - OREF (213):

Romoser et al., Detection in living cells of Ca2 +-dependent changes in the fluorescence emission of an indicator composed of two green fluorescent protein variants liked by a calmodulin-binding sequence, J. of Biolog. Chem. 272(20):13270-13274 (1997).

US-PAT-NO: 6627275

DOCUMENT-IDENTIFIER: US 6627275 B1

TITLE: Tear resistant elastic crystal gels suitable for inflatable restraint cushions and other uses

DATE-ISSUED: September 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chen; John Youngfu	Pacifica	CA	N/A	N/A

APPL-NO: 09/ 130545

DATE FILED: August 8, 1998

PARENT-CASE:

RELATED APPLICATIONS

This application is a continuation-in-part of the following applications: U.S. Ser. Nos: 08/984,459, filed Dec, 3, 1997; 08/909,487, filed Jul. 12, 1997; 8/863,794, fied May 27, 1997; 08/819,675 filed Mar. 17, 1997 now U.S. Pat. No. 5,884,639 ; PCT/US97/17534, filed Sep. 30, 1997; U.S. Ser. No: 08/719,817 filed Sep. 30, 1996, U.S. Ser. No: 08/665,343 filed Jun. 17, 1996,which is a Continuation-in-part of U.S. Ser. No: 08/612,586 filed Mar. 8, 1996 PCT/US94/04278 filed Apr. 4, 1994 (published May 26, 1995 No. WO95/13851); PCT/US94/07314 filed Jun. 27, 1994 (published Jan. 4, 1996 No. WO 96/00118); Ser. No. 08/288,690 filed Aug. 1, 1994 now U.S. Pat. No. 5,633,286; Ser. No. 08/581,188 filed Dec. 29, 1995 now abandoned ; Ser. No. 08/581,191 filed Dec 29, 1995 now U.S. Pat. No. 5,760,177 ;Ser. No. 08/581,125 filed Dec. 29, 1995. In turn U.S. Ser. Nos.08/581,188; 08/581,191; and 08/581,125 are continuation-in-parts of the following applications: Ser. Nos.: 08/288,690, filed Aug. 11, 1994 now U.S. Pat. No. 5,633,286, PCT/US94/07314 filed Jun. 27, 1994 (CIP of PCT/US 94/04278, filed Apr. 19, 1994 which in turn is a CIP of Ser. No. 07/957,290 U.S. Pat. No. 5,334,646 filed Oct. 10, 1992); The above patents and applications are specifically incorporated herein by reference.

US-CL-CURRENT: 428/35.2, 280/728.1

ABSTRACT:

An airbag copmrising crystal gels is disclosed. The crystal gel comprises one or more block copolymers having at least one crystalline midblock and high levels of a plasticizer. The midblock segment has an amount of crystallinity sufficient to achieve improvements in one or more physical properties including improved crack propagation resistance, improved tear resistance, improved resistance to fatigue and resistance to catastrophic failure.

6 Claims, 150 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 21

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Brief Summary Text - BSTX (24):

The crystal gels of the invention can be formed into gel strands, gel tapes, gel sheets, and other articles of manufacture. Moreover, because of their improved tear resistance and resistance to fatigue, the crystal gels exhibit versatility as balloons for medical uses, such as balloon for valvuloplasty of the mitral valve, gastrointestinal balloon dilator, esophageal balloon dilator, dilating balloon catheter use in coronary angiogram and the like. Since the crystal gels are more tear resistant, they are especially useful for making condoms, toy balloons, and surgical and examination gloves. As toy balloons, the crystal gels are safer because it will not rupture or explode when punctured as would latex balloons which often times cause injures or death to children by choking from pieces of latex rubber. The crystal gels are advantageously useful for making gloves, thin gloves for surgery and examination and thicker gloves for vibration damping which prevents damage to blood capillaries in the fingers and hand caused by handling strong shock and vibrating equipment.

Detailed Description Text - DETX (60):

The crystal gels can also contain useful amounts of conventionally employed additives such as stabilizers, antioxidants, antiblocking agents, colorants, fragrances, flame retardants, flavors, other polymers in minor amounts and the like to an extend not affecting or substantially decreasing the desired properties. Additives useful in the crystal gel of the present invention include: tetrakis[methylene 3,-(3T51-di-tertbutyl-4"-hydroxyphenyl) propionate] methane, octadecyl 3-(3", 5"-di-tert-butyl-4"-hydroxyphenyl) propionate, distearyl-pentaerythritol-diproprionate, thiodiethylene bis-(3,5-ter-butyl-4-hydroxy) hydrocinnamate, (1,3,5-trimethyl-2,4,6-tris[3,5-di-tert-butyl-4-hydroxybenzyl] benzene), 4,4"-methylenebis(2,6-di-tert-butylphenol), steraric acid, oleic acid, stearamide, behenamide, oleamide, erucamide, N,N"-ethylenebisstearamide, N,N"-ethylenebisoleamide, sterryl erucamide, erucyl erucamide, oleyl palmitamide, stealryl stearamide, erucyl stearamide, calcium sterate, other metal sterates, waxes (e.g., polyethylene, polypropylene, microcrystalline, carnauba, paraffin, montan, candelilla, beeswax, ozokerite, ceresine, and the like), teflon (TFE, PTFE, PEA, FEP, etc), polysiloxane, etc. The crystal gel can also contain metallic pigments (aluminum and brass flakes), Tio2, mica, fluorescent dyes and pigments, phosphorescent pigments, aluminatrihydrate, antimony oxide, iron oxides (Fe3O4,--Fe2O3, etc.), iron cobalt oxides, chromium dioxide, iron, barium ferrite, strontium ferrite and other magnetic particle materials, molybdenum, silicones, silicone fluids, lake pigments, aluminates, ceramic pigments, ironblues, ultramarines, phthalocynines, azo pigments, carbon blacks, silicon dioxide, silica, clay, feldspar, glass microspheres, barium ferrite, wollastonite and the like. The report of the committee on Magnetic Materials, Publication NMAB-426, National Academy Express (1985) is incorporated herein by reference.

Detailed Description Text - DETX (64):

The crystal gels are prepared by blending together the components including other additatives as desired at about 23.degree. C. to about 100.degree. C. forming a paste like mixture and further heating said mixture uniformly to about 150.degree. C. to about 200.degree. C. until a homogeneous molten blend is obtained. Lower and higher temperatures can also be utilized depending on the viscosity of the oils and amounts of multiblock copolymers (I) and polymer (II) used. These components blend easily in the melt and a heated vessel

equipped with a stirrer is all that is required. Small batches can be easily blended in a test tube using a glass stirring rod for mixing. While conventional large vessels with pressure and/or vacuum means can be utilized in forming large batches of the instant crystal gels in amounts of about 40 lbs or less to 10,000 lbs or more. For example, in a large vessel, inert gases can be employed for removing the composition from a closed vessel at the end of mixing and a partial vacuum can be applied to remove any entrapped bubbles. Stirring rates utilized for large batches can range from about less than 10 rpm to about 40 rpm or higher.

Detailed Description Text - DETX (74):

Because of their improved tear resistance and resistance to fatigue, the crystal gels exhibit versatility as balloons for medical uses, such as balloon for valvuloplasty of the mitral valve, gastrointestinal balloon dilator, esophageal balloon dilator, dilating balloon catheter use in coronary angiogram and the like. Since the crystal gels are more tear resistant, they are especially useful for making condoms, toy balloons, and surgical and examination gloves. As toy balloons, the crystal gels are safer because it will not rupture or explode when punctured as would latex balloons which often times cause injures or death to children by choking from pieces of latex rubber. The crystal gels are advantageously useful for making gloves, thin gloves for surgery and examination and thicker gloves for vibration damping which prevents damage to blood capillaries in the fingers and hand caused by handling strong shock and vibrating equipment.

US Reference Patentee Name - URNM (28):

Toy

US Reference Patentee Name - URNM (63):

Toy

US Reference Group - URGP (28):

4721832 19880100 Toy 174/87

US Reference Group - URGP (63):

5177143 19930100 Toy 524/848

US-PAT-NO: 6617588

DOCUMENT-IDENTIFIER: US 6617588 B1

TITLE: Photosonolysis for decomposition of toxics in water

DATE-ISSUED: September 9, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sato; Chikashi	Pocatello	ID	N/A	N/A

APPL-NO: 09/ 288595

DATE FILED: April 8, 1999

PARENT-CASE:

This application is a conversion of, a continuation-in-part of, and claims priority from, prior pending provisional application serial No. 60/081,267, filed on Apr. 8, 1998 with the same title, which is incorporated herein by reference.

US-CL-CURRENT: 250/455.11, 210/748 , 422/186.3

ABSTRACT:

The invention is a process and reactors designs for simultaneous ultraviolet light/ultrasound(UV/US) treatment of halogenated organic compounds contaminants in water. The reactors are preferably circular cylindrical reaction vessels that accept a central ultrasonic horn. UV light is provided by lamps placed generally parallel to the reactor walls. Or, UV light may be centrally provided in an immersion well near the ultrasonic horn. This way, simultaneous UV/US energy may be effectively provided to the reactors for the remediation of toxic compounds in the water in the reactors. Also, this way, compact and portable reactors may be constructed to permit mobile applications of the UV/US processes.

1 Claims, 13 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 11

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Brief Summary Text - BSTX (8):

Photolysis occurs competitively with the radiation and radiationless reactions. In the former reaction, the molecules's extra energy is released through emission of light (e.g., fluorescence). In the latter reaction, its extra energy is converted to thermal energy and dissipated. The absorption of light energy by the molecule may occur directly or indirectly. When the molecule itself directly adsorbs light energy and is degraded, the reaction is direct photolysis, while light energy is transferred from other substances, the resulting reaction is indirect or sensitized photolysis. When photons of light strike a semiconductor, they are either absorbed or scattered. The absorbed

photons with energy greater than or equal to the semiconductor band gap energy excite electrons from the valence band to the conduction band. The excitation generates electron-hole pairs (e.sup.- +h.sup.+) on semiconductors, which can either recombine and release heat, or cause oxidation and reduction reactions by charge transfer to species adsorbed to the semiconductor (Lau, 1996).

Brief Summary Text - BSTX (9):

Sonolysis is a physical/chemical reaction initiated by implosion of cavitation bubbles in liquid, induced by ultrasound. Ultrasound can create powerful rarefaction waves to develop a negative pressure in liquid. If the waves are powerful enough to overcome the intermolecular forces of bonds in liquid, the liquid molecules will be torn apart from each other to form microbubbles in liquid. The cavitation bubbles are formed at the weak spots in the liquid. Once a microbubble is formed, it rapidly grows until it reaches the critical size at which the bubble can no longer sustain itself and results in an implosion instantaneously releasing a large amount of energy (Bhatnagar and Cheung, 1994).

Brief Summary Text - BSTX (10):

The energy generated by the compression of gas and vapor inside is released as intense heat at a local hot spot. Suslick (1990) reported that these hot spots (imploding bubbles) would reach temperature of 5000.degree. C., pressure of 500 atmospheres, and heating and cooling rates greater than 10.sup.9 K/sec. Thus, the reaction that takes place in aqueous solution may be direct bond cleavage, or thermal reaction similar to combustion. The extreme conditions may also produce reactive species (e.g., H.sub.2 O.sub.2, HO.sub.2., .H, .OH) in aqueous solution, and result in hydrolysis and oxidation-reduction reactions with these species.

Brief Summary Text - BSTX (11):

Photosonolysis is the use of photolysis and sonolysis in combination. Initial studies on the use of photosonolysis were reported by Toy and Stringham (1984, 1985). They used ultraviolet light (UV) and ultrasonic waves (US) for the synthesis of 1,2,4-tris(methylthio)-3-H-hexafluoro-n-butane from methyl disulfide and hexafluorobutadiene. Photosonolysis was later applied in numerous additional synthetic applications, and has also been applied to polymer degradations (Toy and Stringham, 1985; Toy et al., 1990).

Brief Summary Text - BSTX (12):

Toy and Stringham's photosonosynthesis work has been expanded by other researchers to the applications to waste remediation technologies. Sierka and Amy (1985) studied the composite effects of ultraviolet light (UV), ultrasound (US), and ozone oxidation (O.sub.3) to reduce the trihalomethane formation potential and maximize the destruction of nonvolatile total organic carbons. They found that concurrent use of UV, US, and ozone provided the most effective combination in the performed experiments.

Brief Summary Text - BSTX (14):

Toy et al. (1990) studied photosonocatalysis on decomposition of ethylene glycol and urea in aqueous solutions, and reported that photosonocatalytic decomposition is more aggressive than with either sonolysis or photolysis individually. Toy et al. (1990) also performed experiments on the photosonochemical decomposition of aqueous 1,1,1-trichloroethane (TCA), and reported that the combined use of photolysis and sonolysis causes a greater

decomposition than if each technique were used separately.

Detailed Description Text - DETX (62):
As was mentioned earlier, experimental conditions were chosen to allow the comparisons between UV, US and UVUS. Optimization to increase reactor efficiency and obtain higher degradation rates was beyond the scope of the present work. It is expected that increasing the power of the UV and US sources will result in higher degradation rates and removal efficiencies. Significantly high concentrations of TiO.sub.2 can result in lower photocatalysis efficiency due to the interference of the solid catalyst with light penetration. Particle size and concentration of TiO.sub.2 also affect the sonolysis rate. Orzechowska et al. suggested that the fine particles may enhance the rate by providing additional nuclei for bubble formation and large particles may decrease the rate because of sound attenuation. They found, however, that sand particles at various sizes and concentrations had a negligible effect on the degradation rate.

Detailed Description Text - DETX (63):
The mechanism of ultrasonic enhancement, when used in combination with TiO.sub.2 -photocatalysis, is thought to be due to acoustic and/or cavitational effects at the semiconductor-solution interface. At the microscopic level, the implosion of vapor bubbles near the semiconductor particle may enhance mass transport at solid surfaces, and aid in surface adsorption of the substrate. Local region of high temperature and pressure can also result in the acceleration of reactions between free radicals and the substrate. Microjets induced by cavitation may act to cleanse the catalyst surface which may become poisoned by inert byproducts. This mechanism may allow more effective adsorption and radical production, and may decrease the effective diffusion zone thickness for reactants and products. In our study, however, enhancement of the VOC photolysis by US was observed in the experiments with and without TiO.sub.2 particles, suggesting that direct- or noncatalytic-photolysis was the predominant reaction. If the photolysis rate (k) is a direct function of the light intensity (I.sub..lambda.), molar absorbtivity (.epsilon..sub..lambda.) at wavelength .lambda., and quantum yield (.phi.) of the compound of interest, the quantum yield might possibly be a cause for the observed synergism. It can be postulated that photolysis, in combination with sonolysis, initiated a chain reaction for the VOC degradation, resulting in increased quantum yield. Without more evidence, the ultrasonic enhancement mechanisms that produce the synergistic effect in the photolysis of VOC compounds remains an open question.

Other Reference Publication - OREF (1):
Toy & Stringham, "Ultrasonic Photolysis of Methyl Disulfide and Hexafluorobutadiene", 1984, Journal of Fluorine Chemistry 25, pp 213-218.

Other Reference Publication - OREF (3):
Toy & Stringham, "Photosonosynthesis of 1,2,4-Tris(Methylthio)-3-H-Hexafluoro-n-Butane", 1985, Journal of Fluorine Chemistry29, pp. 253-260.

Other Reference Publication - OREF (4):
Toy, Carter & Passell, "Photosonochemical Decomposition of Aqueous 1,1,1 -Trichloroethane", 1990, Environmental Technology, vol. 11, pp. 837-842.

Other Reference Publication - OREF (5):

Toy, Scheppers & Passell, "Photosonocatalysis on Decomposition of Some Organics in Aqueous Solutions", Apr. 27, 1990, 199.sup.th National Meeting of American Chemical Society, Report No. CONF-900402, pp. 384-387.

US-PAT-NO: 6612712

DOCUMENT-IDENTIFIER: US 6612712 B2

TITLE: Lighting system and device

DATE-ISSUED: September 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Nepil; James	Garfield	NJ	07026	N/A

APPL-NO: 10/ 005761

DATE FILED: November 12, 2001

US-CL-CURRENT: 362/101, 362/318 , 362/806 , 362/96

ABSTRACT:

The present invention is a light-producing technology exemplified by lighting that is safe, reliable, energy efficient, long lasting, and capable of operating under a wide range of weather and other conditions. The device incorporates a durable housing, a light element, a liquid solution, and a power supply. Subject only to its power source, it is capable of indefinitely producing intensely visible light at 100 yards or more during both daytime and nighttime. It can be configured for higher or lower intensities in a wide variety of foreseen applications. The device is not flammable, explosive, or toxic, and without loss of function withstands shock, extended water immersion, and heating and cooling to temperatures below freezing and approaching boiling.

20 Claims, 3 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 1

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Brief Summary Text - BSTX (9):

The device of U.S. Pat. No. 4,967,321 to Cimock is a flashlight wand designed as a children's toy. The wand contains two DC batteries, a small incandescent bulb, and light reflecting objects. Light production of the Cimock device is limited. U.S. Pat. No. 5,392,203 to Harris, Jr. discloses a waterproof taxi light to guide aircraft on a tarmac. The device includes a lighted signal member with an elongate, translucent tubular member adapted for providing both daytime and nighttime illumination. The light source is a DC battery powered flashlight bulb. The translucent tube provides for light dispersion. Harris, Jr. discloses the use of a clear fluid within the translucent tubular member (column 6, lines 10-15), but the light element, a bulb, is not even partially submerged in the fluid. Thus, the light is not as intense as it could be if the light element were at least partially submerged in the fluid.

Brief Summary Text - BSTX (11):

U.S. Pat. No. 4,070,777 to Lo Giudice discloses a novelty display device incapable of producing intensely visible light. Designed for amusement, this device uses miniature lamps strung through the length of a liquid-filled housing to illuminate a continuous flow of bubbles through a liquid contained within a hollow glass tube. Boiling liquid heated by lighted bulbs is the bubble source. The device is not only an inadequate means of producing high intensity lighting, but it is also not durable because the glass housing will likely shatter if dropped. U.S. Pat. No. 4,271,458 to George, Jr. discloses decorative light tubing for lighted tube displays. The device comprises a flexible tube containing a dielectric fluid (such as mineral oil or glycerin) and low voltage filament bulbs. However, this device is incapable of producing high-intensity lighting.

Brief Summary Text - BSTX (12):

U.S. Pat. No. 4,600,974 to Lew et al. discloses an optically decorated light baton with multiple purposes similar to the present prototype. It is a portable light tube with reflective platelets suspended in a medium, and in one embodiment phosphorescent or fluorescent material coats the light-emitting tube. The device of U.S. Pat. No. 5,165,781 to Orak is a novelty flashlight with color producing chambers intended for use as a toy or amusement. It comprises a low heat generating filament bulb and colored-fluid-containing transparent cups mounted to a power receiving housing. The light is not intensely visible because the bulb is at one end of the housing, which itself lacks fluid. The device requires continuous agitation to swirl the liquid colors. Although the housings of these two devices are fluid-filled, the light is not intensely visible partly because the light sources are located at only one end of the device where there is no fluid. Furthermore, although both devices utilize fluid mediums, both require agitation to obtain the full effect of the fluid: the Orak device requires agitation to swirl the liquid colors and the Lew et al. device requires agitation to make the light reflecting particles move through the fluid.

Brief Summary Text - BSTX (13):

U.S. Pat. No. 5,662,406 to Mattice discloses a lighted baby bottle designed for easy location in the dark. A filament bulb produces a low intensity glowing light and some heat. U.S. Pat. No. 5,993,021 to Lin discloses a decorative lamp designed for aquarium accent lighting. A tube containing water and artificial fish is illuminated by a low-intensity, heat-producing filament bulb not immersed in the fluid. A bubble valve produces air bubbles which cause the artificial fish to move.

Brief Summary Text - BSTX (19):

Briefly described, in a preferred form, the present invention comprises a new light-generating technology, and lighting devices that incorporate the technology. The light-generating technology incorporates the use of a fluorescent dye dissolved in a fluid medium that at least partially surrounds the light element. The preferred lighting device utilizing this lighting principal comprises a durable housing, a light element, a power source for the light element, and a lighting fluid at least partially surrounding the light element.

Brief Summary Text - BSTX (20):

The device is lightweight, safe, durable, long lasting, and energy efficient. The present lighting device incorporates the following characteristics, among others, which distinguish the invention from the prior

art: (a) the new lighting principle--fluorescent dye dissolved in a fluid medium; (b) high energy efficiency--high light intensities generated by low power (AC or DC); (c) long operational life--subject only to power supply, light emission continues indefinitely without chemical breakdown or materials fatigue; (d) adjustable light intensity--by composition of the fluid medium and control of the power source; (e) simple construction--few parts to fail; and (f) durable construction--water-submersible and shock-proof, virtually unbreakable in normal use.

Brief Summary Text - BSTX (22):

The light-emitting section comprises an LED secured to the housing and at least partially submerged in a lighting fluid. In a preferred form, the device comprises four LEDs for sufficient light intensity, and the lighting fluid comprises a solution of approximately 10 ml water, 7 ml of 80 proof vodka as a non-toxic ethanol source, and 5 ml of water-soluble, non-toxic, fluorescent color from Createx Colors of East Granby, Conn. The lighting fluid preferably fills approximately 7/8ths of the light-emitting section, leaving approximately 1/8.sup.th of the section as air space. Coolants of the lighting fluid can be other than alcohol, for example de-icing fluid Types 1 and 4. While these are toxic, they can be used with or without aqueous dilution with water. It will be understood by those of skill in the art that ingredient concentrations can vary to produce different effects and intensities, although some combinations may have disadvantageous effects. For example, as more color is used, the more likely it is to adhere to the LEDs, causing a rise in temperature.

Brief Summary Text - BSTX (26):

The present invention is superior to prior art devices in numerous ways. The following examples are specific distinguishing features of the present invention and the above-described prior art. The present invention differs from the Harris, Jr. light in its use of LEDs in a fluorescing fluid as an integral part of a lighting principle. The Harris, Jr. device is not submergible, nor as durable as the present invention. The present devices differ from that of Harris, Jr. in that their body is filled with a mixture of ethanol, water, and fluorescent dye, and has LEDs as the light source. The LEDs are pushed to a controllably higher voltage limit than they were designed for because the fluid serves as a coolant in addition to dispersing the light. The filament bulb of the Harris, Jr. device draws high power vs. that of the present devices' LEDs, but emits a much lower intensity of usable light. Compared to light bulbs, LEDs are less subject to breakage in use and have a far longer life span. In fact, the design of the present invention was prompted by use of a Harris, Jr. type device under harsh airport conditions where it failed under temperature extremes, and broke when dropped or exposed to vibration. Harris, Jr. discloses that a clear liquid could be used in its fluidless device, but the reason for this is unclear as the bulb of Harris, Jr. would fail under immersion. Finally, the Harris, Jr. design has limited use, not the broad applications foreseen for the technology of the present application.

Brief Summary Text - BSTX (27):

The Lew et al. device differs from the present invention in having incandescent vs. LED light sources, reflective platelets in the medium, a phosphorescent or fluorescent surface coating (if present) vs. dissolved in the fluid, and it must be agitated or mixed during use to make the light reflecting particles move through the medium. Further, only low light intensities are generated.

Brief Summary Text - BSTX (32):
An object of the present invention is to disclose a new lighting principle--fluorescent dye dissolved in a fluid medium;

Detailed Description Text - DETX (7):
In one preferred embodiment, the lighting fluid 40 is a solution often (10) parts of water, seven (7) parts of 80-proof vodka, and five (5) parts of water-soluble, non-toxic, fluorescent color from Createx Colors. However, the concentrations can be varied. Alternatively, as will be understood by those of skill in the art, other materials such as glycol, salt, and isopropyl alcohol can be used. Preferably, the lighting fluid 40 contains no particulate matter so the emitted light is not reflected or refracted in the lighting fluid 40. However, the lighting fluid 40 can contain other material, whether soluble or not. Alternatively, the lighting fluid 40 can be other gaseous or liquid substance or any combination of such substances that provide some element of durability to the device 10 and/or additional luminosity. The lighting fluid 40 preferably fills 7/8ths of the light-emitting section 24, leaving 1/8th as air space. However, these proportions can be varied.

Claims Text - CLTX (1):
1. A lighting device comprising: (a) a light-emitting section through which visible light can pass; (b) a medium carried by the light-emitting section; and (c) a light element at least partially submerged in the medium, wherein the medium includes fluorescent color dye.

Claims Text - CLTX (2):
2. The lighting device of claim 1, wherein the medium is a fluid comprising water, a coolant, and the fluorescent color dye.

Claims Text - CLTX (5):
5. The lighting device of claim 1, wherein the medium is a fluid wherein the fluorescent color dye is dissolved in the fluid medium, and wherein the fluid medium at least surrounds the light element.

Claims Text - CLTX (9):
9. The lighting device of claim 6, wherein the coolant is selected from the group consisting of ethanol and dc-icing fluid Types 1 and 4, and wherein the color dye is fluorescent dye.

Claims Text - CLTX (13):
13. A method of lighting an area with visible light comprising the following steps: (a) at least partially submerging a light element in a medium contained within a light-emitting section of a housing, the light-emitting section of the housing enabling visible light to pass there through; (b) fixedly securing the light element in the medium; and (c) energizing the light element, wherein the medium includes fluorescent color dye.

Claims Text - CLTX (14):
14. The method of lighting according to claim 13, wherein the medium is a fluid comprising water, a coolant, and the fluorescent color dye.

Claims Text - CLTX (16):

16. The method of lighting according to claim 14, wherein the fluid comprises approximately ten parts water, approximately seven parts coolant, and approximately five parts soluble fluorescent color dye.

US-PAT-NO: 6599444

DOCUMENT-IDENTIFIER: US 6599444 B2

TITLE: Luminescent gel coats and moldable resins

DATE-ISSUED: July 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Burnell-Jones; Peter	Burleigh Gardens	N/A	N/A	AU

APPL-NO: 09/ 766415

DATE FILED: January 18, 2001

PARENT-CASE:

This application is a divisional of prior application Ser. No. 09/170,432, filed Oct. 13, 1998, now U.S. Pat. No. 6,207,077.

US-CL-CURRENT: 252/301.36, 252/500 , 252/513 , 428/690

ABSTRACT:

Luminescent polymers are prepared from thermosetting unsaturated polyesters, suspending fillers and phosphorescent pigments and utilized to make gel coated articles and molded, cast and fiberglass reinforced plastic (FRP) articles. The luminescent polymers show bright and long-lasting photoluminescent afterglow, strong thermostimulation of afterglow by heat and electroluminescent properties. The preferred thermosetting unsaturated polyester resins are prepared by condensing mixtures of ethylenically unsaturated and aromatic dicarboxylic acids and anhydrides with dihydric alcohols and a polymerizable vinylidene monomer. Preferred suspending fillers and thixotropic modifiers include silica, microspheres, glass fibers and other short fibers, nepheline syenite, feldspar, mica, pumice, magnesium sulfate, calcium carbonate, bentonite and the various clays and thixotropic modifiers and mixtures thereof. Preferred phosphorescent pigments include alkaline earth aluminate phosphors, zinc sulfide phosphors and mixtures of these phosphors.

6 Claims, 0 Drawing figures

Exemplary Claim Number: 1

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Brief Summary Text - BSTX (6):

Examples of luminescence are the dim glow of phosphorus (a chemiluminescence), the phosphorescence of certain solids (phosphors) after exposure to sunlight, X-rays or electron beams, the transitory fluorescence of many substances when excited by exposure to various kinds of radiation, the aurora borealis and the electroluminescence of gases when carrying a current, the triboluminescence of crystals when rubbed or broken, the bioluminescence of many organisms, including the firefly, the glowworm and the "burning of the sea," the fungus light of decaying tree trunks, and the bacterial light of dead flesh or fish.

Detailed Description Text - DETX (83):
Another group of materials that has been found to be useful in conjunction to brighten and improve reflective qualities with the present invention are luminescence enhancers such as optical brighteners, fluorescent whiteners, color brighteners and spectrum enhancers. Fluorescent daylight pigments are particularly effective in conjunction with UV stabilizers and benefit from UV protection.

Detailed Description Text - DETX (84):
Other materials that may prove useful with the present invention include coral extracts, isolates and derivatives for UV protection, daylight fluorescent pigments, pearlescent pigments, metallic flake pigments, thermochromics (producing heat-activated color changes), photochromics (producing light-activated color changes), diamond-like materials from solutions of polyphenylcarbyne, color concentrates, etc.

Detailed Description Text - DETX (87):
JS AQUAGUARD Culture Finish/Clear Gelcoat is a clear polyester/styrene gel coat used as a topcoat for swimming pools containing fumed silica, benzophenone and/or phenolic UV inhibitors and metal naphthenates and octoates as activators. ESCON EX80 (61-286), obtained from FGI of Australia, is a low viscosity, low reactivity, high clarity, acrylic modified polyester resin designed for decorative castings and embedding where excellent color and clarity are desired. ESCON EX80 is supplied pre-accelerated and stabilized to minimize discoloration and deterioration by UV light. On the addition of 1% MEKP at 25.degree. C. a gel time of from 45-60 minutes can be expected. Curing proceeds relatively slowly once the resin has gelled; very low exotherm (approximately 40-50.degree. C.) characteristics give a slow even cure over a period of several hours, ensuring that cracking and discoloration due to overheating is avoided in larger casting. The low viscosity of ESCON EX80 is advantageous in allowing fast release of air bubbles before gelation occurs. Post curing of the finished article is essential.

Detailed Description Text - DETX (104):
LUMILUX.RTM. Green SN-pigments, available from Riedel-de Haen of Germany, are a long-lasting afterglow luminescent alkaline earth aluminate doped with rare earths. LUMILUX.RTM. Green SN-pigments have an excitation maximum of 380 to 400 nm, an emission maximum of 520 nm and a density of approximately 3.5 g/ml. The afterglowing effect is around ten times brighter than that of the classical zinc sulfides such as the LUMILUX.RTM. Green N-PM 50090 described above, with a duration of afterglow (down to 0.3 mcd/m.sup.2) of up to 3600 minutes. The initial radiant intensity of the afterglow can be increased by up to 30% when excitation is carried out with illumination levels of 3000 to 5000 Lux instead of the usual 1000 Lux. The LUMILUX.RTM. Green SN-pigments are stable against greying but are sensitive to water. They are sensitive to spectral excitation beginning in the blue part of the visible spectrum and extending up to well into the longwave UV wavelengths. If the level of illumination available for excitation is low (<300 Lux) or if only a filament bulb is available, the afterglow effect is of a very much reduced level even if "charging" is carried out for a very long time. The maximum afterglow effect is produced with excitation by daylight or high strength, cold-white fluorescent lamps. LUMILUX.RTM. Green SN-FO 50069 has a density of 3.4 g/cm.sup.3, a screen discharge size of less than 80 .mu.m (less than 1% oversized particles) and a particle size distribution d.sub.50 of 40 .mu.m.+-.4

.mu.m. The excitation spectrum has a maximum at approximately 370 nm, with a phosphorescence spectra maximum at approximately 520 nm. LUMILUX.RTM. Green SN-FOG 50089 has similar properties with a screen discharge size of less than 125 .mu.m (less than 1% oversized particles) and a particle size distribution d.sub.50 of 50 .mu.m.+-.5 .mu.m.

Detailed Description Text - DETX (107):
UMC Phosphorescent pigments, available from United Mineral & Chemical Corp., are sulfide based pigments available in a variety of emission colors and daylight fluorescent colors. UMC 6SSU is a ZnS:Cu phosphor with an emission peak at 529.+-.4 a specific gravity of 4.1 and an average particle size of 22. UMC GSR is a yellow emitting ZnS:Cu,Mn phosphor with emission peaks at 520 and 570, a specific gravity of 4.1 and an average particle size of 22 nm. UMC BAS is a (Ca,Sr)S:Bi blue emitting phosphor with emission peaks at 450 and 580, a specific gravity of 3.2 and an average particle size of 35 nm.

Detailed Description Text - DETX (111):
UVITEX.RTM. OB is a Ciba Specialty Chemicals fluorescent whitening agent. It is a high molecular weight low volatility optical brightener of the thiophenediyl benzoxazole class (2,5-thiophenediylbis(5-tert-butyl-1,3-benzoxazole)). UVITEX OB has exceptional whitening properties, good light fastness and a brilliant bluish cast (an absorption peak at .about.380 nm and an emission peak at .about.430 nm. The use levels of UVITEX OB range between 0.005-0.1% depending on performance requirements of the final application. Basically, the brightening effect is not light stable. It may be used in a variety of blends and combinations with other UV stabilizers and optical brighteners; the concentration of UVITEX OB should be increased when combined with the TINUVIN UV stabilizers discussed herein.

Detailed Description Text - DETX (125):
UV stabilizers, spectrum enhancers, fluorescent whitening agents and/or optical brighteners are added before or after the LUMILUX.RTM.. If the mixture appears slightly "floury," they are preferably added before the phosphorescent pigment. If the mixture is "watery," they should be added afterwards. Otherwise, they are added in split portions before and after the phosphors. UV stabilizers and luminescence enhancers may be utilized in percentages ranging fro 0.1-3.0 percent, with the lower ranges of UV stabilizer being preferred when alkaline earth aluminate oxide phosphors are utilized and the upper ranges being utilized with zinc sulfide phosphor (and mixes of phosphors containing ZnS) and luminescence enhancers.

Detailed Description Text - DETX (157):
Examples of the invention described above have been made and tested and found to deliver the advantages described. The luminescent polymers have been utilized as a gel coat on items including automobiles, hubcaps, bicycles (frame and wheel rims), signs, boats (exterior trim), trailers, outboard motor covers, fishing poles and banners. The luminescent polymers have been further utilized to mold items including safety and bicycle helmets, a dinghy runabout boat, house numbers and letters, keys for musical keyboards, skateboards, scratchplates for guitars, light switch and door handle surrounds, doors, smoke detector covers, knife and tool handles, telephones, floor tiles, ceiling and wall panels, stair treads, seat inserts and table tops, printed circuit boards, headlight and light reflectors, solar cell lens, spa baths and vanity basins, watch and clock faces, cats eye road markers, mouse and rat traps, flying

insect catchers, walking sticks, lamp stands, remote controlled car bodies, battery covers for trucks, fishing lures, fiberglass rocks for use in spas and novelty items. Flexible items made and tested have included fishing nets, clothing and ship's pennants.

US-PAT-NO: 6531230

DOCUMENT-IDENTIFIER: US 6531230 B1

TITLE: Color shifting film

DATE-ISSUED: March 11, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Weber; Michael F.	Shoreview	MN	N/A	N/A
Nevitt; Timothy J.	Red Wing	MN	N/A	N/A
Merrill; William W.	White Bear Lake	MN	N/A	N/A
Roscoe; Kelly M.	Orono	MN	N/A	N/A
Ouderkirk; Andrew J.	Woodbury	MN	N/A	N/A
Wheatley; John A.	Lake Elmo	MN	N/A	N/A
Hanson; Gary B.	Hudosn	WI	N/A	N/A
Jonza; James M.	Woodbury	MN	N/A	N/A
Boettcher; Jeffrey A.	Falcon Heights	MN	N/A	N/A
Liu; Yaoqi J.	Maplewood	MN	N/A	N/A
Neavin; Terence D.	St. Paul	MN	N/A	N/A

APPL-NO: 09/ 006591

DATE FILED: January 13, 1998

US-CL-CURRENT: 428/480, 428/357 , 428/577 , 428/580 , 428/584 , 428/589

ABSTRACT:

Multilayer polymeric films and other optical bodies are provided which is useful in making colored mirrors and polarizers. The films are characterized by a highly uniform change in color as a function of viewing angle.

10 Claims, 49 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 28

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Detailed Description Text - DETX (208):

Local random color variations can also be achieved by extruding films of the present invention with small internal bubbles to produce attractive decorative effects. Bubbles can be created by several methods including not drying the resin as sufficiently as one would normally do, or by slightly overheating a thermally sensitive resin such as PMMA to create a similar effect. The small bubbles formed locally distort the microlayers and cause a local color change which can give the appearance of depth in some instances.

Detailed Description Text - DETX (270):

In addition to the above, for good color rendition, it is preferable for the average transmission in the stop band to be less than about 10% and to have no passbands within said stopband whose peak transmission values are greater than

about 20%. More preferably, the average transmission in the stop band is less than about 5% and the maximum transmission of a passband peak within a stopband is about 10%. The restriction on leaks is important, even as applied to narrow spectral leaks that may occur in a stop band. When combined with certain narrow band emission sources such as low pressure sodium lamps or certain fluorescent lamps, a large percentage of the light source energy can be transmitted through a narrow band leak in a stopband.

Detailed Description Text - DETX (325):

Each sample was placed on a Graphiclite D5000 Standard Viewer diffuse backlight, and transmission was measured for the sample with a spectrophotometer using a fiber optic collector that had a numerical aperture of 0.22. The fiber was placed directly on the film perpendicular to the plane of the film sample, thereby allowing light to enter the fiber from the source and through the bare film at angles no greater than 25 degrees from normal. The bare film sample was measured using a baseline of 100% transmission at all wavelengths if the backlight alone was measured. Color values were also calculated for the sample in L*, a*, b* color space, assuming illumination by a compact fluorescent bulb. The films of EXAMPLES E8-1, E8-3, and E8-5 appeared blue, magenta, and yellow, respectively, at normal incidence.

Detailed Description Text - DETX (431):

In the simplest case, the color shifting film of the present invention is used as a filter in a backlit light fixture. A typical fixture contains a housing with a light source and may include a diffuse or specular reflective element behind the light source or covering at least some of the interior surfaces of the optical cavity. The output of the light fixture typically contains a filter or diffusing element that obscures the light source from direct viewing. Depending upon the particular application to which the light fixture is directed, the light source may be a fluorescent lamp, an incandescent lamp, a solid-state or electroluminescent (EL) light source, a metal halide lamp, or even solar illumination, the latter being transmitted to the optical cavity by free space propagation, a lens system, a light pipe, a polarization preserving light guide, or by other means as are known to the art. The source may be diffuse or specular, and may include a randomizing, depolarizing surface used in combination with a point light source. The elements of the light fixture may be arranged in various configurations and may be placed within a housing as dictated by aesthetic and/or functional considerations. Such fixtures are common in architectural lighting, stage lighting, outdoor lighting, backlit displays and signs, and automotive dashboards. The color shifting film of the present invention provides the advantage that the appearance of the output of the lighting fixture changes with angle.

Detailed Description Text - DETX (433):

The color shifting films of the present invention are particularly advantageous when used in directional lighting. High efficiency lamps, such as sodium vapor lamps commonly used in street or yard lighting applications, typically have spectral emissions at only one major wavelength. When such a source which emits over a narrow band is combined with the color shifting film of the present invention, highly directional control of the emitted light can be achieved. For example, when a color shifting film is made with a narrow passband which coincides with the emission peak of the lamp, then the lamp emission can pass through the film only at angles near the design angle; at other angles, the light emitted from the source is returned to the lamp, or lamp housing. Typical monochromatic and polychromatic spikey light sources

include low pressure sodium lamps, mercury lamps, fluorescent lamps, compact fluorescent lamps, and cold cathode fluorescent lamps. Additionally, the reflecting film need not necessarily be of a narrow pass type since, with monochromatic sources, it may only be necessary to block or pass the single wavelength emission at a specific angle of incidence. This means that a reflective film having, for example, a square wave reflection spectrum which cuts on or off at a wavelength near that of the lamp emission can be used as well. Some specific geometries in which the light source and color shifting film of the present invention can be combined include, but are not limited to, the following:

Detailed Description Text - DETX (434):

(a) A cylindrical bulb, such as a fluorescent tube, is wrapped with film designed for normal incidence transmission of the bulb's peak emitted radiation, i.e., the film is designed with a passband centered at the wavelength of the lamp emission. In this geometry, light of the peak wavelength is emitted mainly in a radial direction from the bulb's long axis.

Detailed Description Text - DETX (445):

A bright, colorful display light can be constructed by wrapping a white fluorescent light bulb with a reflective colored film. Several lights were made in this fashion, each with a different colored film, several with a uniformly colored film and two with variably colored film. Samples were made using the films described in EXAMPLES B1-1, E1-1, E1-2, and I6-1. The film was cut to the length of the tube, and was wide enough to wrap around the circumference of the tube once or twice. The number of wraps affects the brightness and the saturation of the colors achieved by controlling the overall transmission of the covering if one wrap is not sufficiently reflective. The variable colored films were made from film of the same run as for EXAMPLE I6-1, but the 49 inch lengths were cut crossweb from the roll instead of down-web. The nonuniformly colored film appeared to shimmer as the viewer walks past, looking like an unstable plasma in a vacuum tube. The purity of the colors in all of the lamps was high enough to give the fluorescent tubes a decidedly "neon" look, with the added effect of a change in color from the center to the periphery of the tube. Only at the center was the normal incidence spectrum observable, even if the viewer were able to walk around the tube and view it from all sides; e.g., a viewer can indefinitely "chase" a peripheral color around a tube and never view that color in the center of the tube. The colored films can be loosely attached or laminated with an adhesive. It was noted that the use of an adhesive to remove the air gap between bulb and film had no noticeable effect on the appearance of the colored tube.

Detailed Description Text - DETX (448):

Most fluorescent bulbs manufactured are straight tubes, with a few being circular or unshaped. The utility of the above described "neon" like tubes would be enhanced for many applications if they could be shaped arbitrarily, and even further enhanced if they were based on a flexible tubular light source. The development of a large core optical fiber by 3M provides such a light source. This product, called the "3M Light Fiber", is available commercially from the Minnesota Mining and Manufacturing Co., St. Paul, Minn. A certain percentage of light in the fiber is scattered past the TIR angle and escapes the fiber. This process can be enhanced by increasing the density of scattering centers in the core or sheath. Also, microstructured film can be attached to the sides of the tube to direct light out of the tubes.

Detailed Description Text - DETX (449):

Samples of both clear and microstructured optical "fiber" of nominally 1 cm diameter was covered with the green/magenta film of EXAMPLE E1-2. The film was first coated with a clear adhesive to make 1 inch wide rolls of colored tape. The adhesive was a hot melt adhesive compounded from a synthetic SIS block copolymer and a hydrocarbon tackifier plus stabilizers. This tape was both spirally wound onto the optical fiber, and linearly applied. Since the 1 inch width did not cover the entire circumference, a strip was applied from both sides in the latter case. The linearly applied strips of tape tended to wrinkle when the fiber was coiled with a radius of less than about 1/3 meter. No wrinkling was observed with the tape on spirally wound fiber, even at 1/6 meter radius of curvature. The colors of the large core optical fibers covered with color shifting tape were the same as observed on the fluorescent tubes. The fibers were illuminated with a small battery powered light. Two or more alternating colors can also be wound with separate spirals, or colored films can be alternated with a broadband "silver" film or alternated with conventional (dye or pigment) colored films or coatings.

Detailed Description Text - DETX (457):

Other articles were made using a collapsible cone of white translucent plastic which was purchased at a toy store and which was made of successively smaller conic sections with the largest attached to a flashlight. Each section was wrapped with colored film of the type described in EXAMPLE B1-1. Alternatively, each section can be wrapped with a different colored film to form a specified color scheme such as, for example, a rainbow sequence. The colored film can also be inserted inside the pre-formed conic sections to better protect the optical film. To retain the angular color change with this latter configuration, optically clear conic sections are preferred.

Detailed Description Text - DETX (464):

Many applications require polarized light to function properly. Examples of such applications include optical displays, such as liquid crystal displays (LCDs), which are widely used for lap-top computers, hand-held calculators, digital watches, automobile dashboard displays and the like, and polarized luminaires and task lighting which make use of polarized light to increase contrast and reduce glare. For some specialized lighting applications, colored polarized light output may be desirable, such as, for example, where both glare reduction and colored "mood" lighting are required. In these situations, polarized task light fixtures with light recycling are preferred for enhanced efficiency. A polarized light fixture generally consists of a housing containing a light source and a polarizing element, and may additionally include a reflecting element and/or a diffusing element. The color shifting film of the present invention can be used as both the polarizing element, and in particular as a reflecting polarizing film (RPF) or as the reflecting element, when present, and particularly as a reflective mirror film (RMF), as described in applicant's copending U.S. Ser. No. 08/418,009 entitled "Polarized Light Sources" and U.S. Ser. No. 08/807,270, entitled "Light Fixture Containing Optical Film", both of which are herein incorporated by reference. For polarized light fixtures incorporating light recycling, a diffuse light source is preferred, which typically includes a light emitting region and a light reflecting, scattering, and/or depolarizing region. The light emitting region may serve both as the light source and the depolarizing region, or the light source may comprise a light emitting region and a separate randomizing reflector. Depending upon the particular application to which the light fixture is directed, the diffuse source may be a fluorescent lamp, an incandescent lamp, a solid-state electroluminescent (EL) light source, or a metal halide lamp, or a separate randomizing, depolarizing surface may be used

in combination with a point light source, a distant light source, or even solar illumination, the later being transmitted to the diffuse polarizer by free space propagation, a lens system, a light pipe, a polarization preserving light guide, or by other means as are known to the art.

Detailed Description Text - DETX (472):

Light sources used in general lighting are often paired to accomplish similar results to the "grow lights". The output wavelengths from some sources actually retard growth, but this can be compensated for by pairing with other sources. For example, low pressure sodium used alone can inhibit synthesis of chlorophyl, but when the low pressure sodium is combined with fluorescent or incandescent lamps, normal photosynthesis occurs. Examples of common pairings of commercial lights used in greenhouses include (i) high pressure sodium and metal halide lamps; (ii) high pressure sodium and mercury lamps; (iii) low pressure sodium and fluorescent and incandescent lamps; and (iv) metal halide and incandescent lamps.

Detailed Description Text - DETX (473):

In a greenhouse environment, the color selective films and optical bodies of the present invention, when used alone as color filters or in combination with reflective backings, are useful for concentrating light of the desired wavelengths for optimal plant growth. The films and optical bodies may be used with normal unfiltered solar light, or they may be combined with artificial broadband light sources to control the wavelength of light emitted from the source. Such light sources include, but are not limited to, incandescent lamps, fluorescent lamps such as hot or cold cathode lamps, metal halide lamps, mercury vapor lamps, high and low pressure sodium lamps, solid-state or electroluminescent (EL) lights, or natural or filtered solar light that is optically coupled to the color selective film. Several filtration/concentration systems will be described in more detail that may be used to manage heat in the greenhouse environment, while delivering an increased amount of light at wavelengths optimized for photosynthesis and other plant photoresponses.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	23151	biolumines$ or fluorescen$ near4 protein$1 or luciferase$1 or photoprotein$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:40
L2	152305	bubble$	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:41
L3	24	1 same 2	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:35
L4	83381	toy or novelty	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:43
L5	46	1 and 2 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L6	28	1 same 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:44
L7	40	1 and toy	US-PGPUB; USPAT	OR	OFF	2004/01/30 11:45
L9	27	7 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L10	34	1 and novelty adj item$1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:53
L11	18	10 not 5	US-PGPUB; USPAT	AND	OFF	2004/01/30 12:00
L12	286	((chemilumines$ or lumines$8 or glow$8) same 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:28
L13	29	((chemilumines$ or lumines$8 or glow$8) near4 2) not 1	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:32
L14	9	12 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:34
L15	0	12 and 2 adj bath	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:34
L16	145975	fluorescen$	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:35
L17	698	16 same 2	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:36
L18	12	17 and 4	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:49
L19	33788	(toy or novelty adj item$1)	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:55
L20	71	16 and 2 and 19	US-PGPUB; USPAT	OR	OFF	2004/01/30 13:55
L21	9343	16 adj protein$1 or gfp	US-PGPUB; USPAT	OR	OFF	2004/01/30 14:08
L22	33	21 and 19	US-PGPUB; USPAT	OR	OFF	2004/01/30 14:08

PGPUB-DOCUMENT-NUMBER: 20040019132

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040019132 A1

TITLE: Bone graft substitutes

PUBLICATION-DATE: January 29, 2004

US-CL-CURRENT: 523/115, 623/23.5

APPL-NO: 10/ 621633

DATE FILED: July 17, 2003

RELATED-US-APPL-DATA:

child 10621633 A1 20030717

parent division-of 09792681 20010223 US GRANTED

parent-patent 6630153 US

[0001] The present invention claims priority to U.S. patent application Ser. No. 09/792,681, filed Feb. 23, 2001, which is incorporated by reference herein in its entirety.

PGPUB-DOCUMENT-NUMBER: 20040018976

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040018976 A1

TITLE: Polynucleotide encoding novel human G-protein coupled receptors, and splice variants thereof

PUBLICATION-DATE: January 29, 2004

US-CL-CURRENT: 514/12, 435/320.1 , 435/325 , 435/69.1 , 530/350 , 530/388.22 , 536/23.2

APPL-NO: 10/ 436715

DATE FILED: May 13, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60380336 20020514 US

[0001] This application claims benefit to provisional application U.S. Serial No. 60/380,336 filed May 14, 2002, under 35 U.S.C. 119(e). The entire teachings of the referenced applications are incorporated herein by reference.

PGPUB-DOCUMENT-NUMBER: 20030232359

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030232359 A1

TITLE: Polynucleotide encoding a novel human G-protein coupled receptor, HGPRBMY40_2

PUBLICATION-DATE: December 18, 2003

US-CL-CURRENT: 435/6, 435/226 , 435/320.1 , 435/325 , 435/69.1 , 536/23.2

APPL-NO: 10/ 391634

DATE FILED: March 18, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60365350 20020318 US

[0001] This application is a continuation-in-part application of provisional application U.S. Serial No. 60/365,350 filed Mar. 18, 2002, and claims benefit of the same under 35 U.S.C. 119(e). The entire teachings of the referenced applications are incorporated herein by reference.

PGPUB-DOCUMENT-NUMBER: 20030185823

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030185823 A1

TITLE: In situ immunization

PUBLICATION-DATE: October 2, 2003

US-CL-CURRENT: 424/144.1, 424/93.7

APPL-NO: 10/ 222960

DATE FILED: August 16, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60313164 20010817 US

[0001] This application claims priority to U.S. Provisional Application Serial No. 60/313,164 filed Aug. 17, 2001, the entirety of which is incorporated by reference herein.

PGPUB-DOCUMENT-NUMBER: 20030154502

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030154502 A1

TITLE: Universal markers of transgenesis

PUBLICATION-DATE: August 14, 2003

US-CL-CURRENT: 800/8, 800/14 , 800/19 , 800/20 , 800/21

APPL-NO: 10/ 360222

DATE FILED: February 7, 2003

RELATED-US-APPL-DATA:

child 10360222 A1 20030207

parent continuation-of 09373129 19990812 US GRANTED

parent-patent 6518481 US

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application claims priority under 35USC120 to U.S. Ser. No. 09/373,129, having the same title and inventors, filed on Aug. 12, 1999, now U.S. Pat. No. 6,518,481, which is incorporated herein by reference.

PGPUB-DOCUMENT-NUMBER: 20030113741

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030113741 A1

TITLE: Apparatus and method for detecting and identifying infectious agents

PUBLICATION-DATE: June 19, 2003

US-CL-CURRENT: 435/6, 435/287.2 , 435/7.9

APPL-NO: 10/ 126777

DATE FILED: April 19, 2002

RELATED-US-APPL-DATA:

child 10126777 A1 20020419

parent division-of 08990103 19971212 US GRANTED

parent-patent 6458547 US

non-provisional-of-provisional 60037675 19970211 US

non-provisional-of-provisional 60033745 19961212 US

RELATED APPLICATIONS

[0001] This application claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional application Serial No. 60/037,675, filed Feb. 11, 1997 and to U.S. Provisional application Serial No. 60/033,745, filed Dec. 12, 1996.

[0002] Certain subject matter in this application is related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS" (B), and to U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES" and to U.S. Provisional application Serial No. 60/023,374, filed Aug. 8, 1996, entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES", and also to published International PCT application No. WO 9?/ ,.

[0003] The subject matter of each of the above noted U.S. applications, provisional applications and International application is herein incorporated by reference in its entirety.

PGPUB-DOCUMENT-NUMBER: 20030092098

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030092098 A1

TITLE: Renilla reniformis fluorescent proteins, nucleic acids encoding the fluorescent proteins and the use thereof in diagnostics, high throughput screening and novelty items

PUBLICATION-DATE: May 15, 2003

US-CL-CURRENT: 435/69.1, 530/350

APPL-NO: 09/ 808898

DATE FILED: March 15, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60189691 20000315 US

RELATED APPLICATIONS

[0001] Benefit of priority under 35 U.S.C. .sctn.119(e) is claimed to U.S. provisional application Serial No. 60/189,691, filed Mar. 15, 2000, to Bryan et al., entitled "RENILLA RENIFORMIS FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS" is claimed.

[0002] This application is related to allowed U.S. application Ser. No. 09/277,716, filed Mar. 26, 1999, to Bruce Bryan and Christopher Szent-Gyorgyi, entitled "LUCIFERASES, FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE LUCIFERASES AND FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS." This application is related to International PCT application No. WO 99/49019 to Bruce Bryan and Prolume, LTD., entitled "LUCIFERASES, FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE LUCIFERASES AND FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS."

[0003] This application is also related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS", now U.S. Pat. No. 5,876,995, issued Mar. 2, 1999, and in U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASTIC TISSUE AND OTHER TISSUES". The application is also related to U.S. application Ser. No. 08/990,103, filed Dec. 12, 1997, to Bruce Bryan entitled "APPARATUS AND METHODS FOR DETECTING AND IDENTIFYING INFECTIOUS AGENTS".

PGPUB-DOCUMENT-NUMBER: 20030066096

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030066096 A1

TITLE: Bioluminescent novelty items

PUBLICATION-DATE: April 3, 2003

US-CL-CURRENT: 800/8, 162/162 , 42/54 , 424/450 , 424/456 , 424/70.14 , 442/131

APPL-NO: 09/ 729133

DATE FILED: December 1, 2000

RELATED-US-APPL-DATA:

child 09729133 A1 20001201

parent continuation-of 09444762 19991122 US PENDING

child 09729133 A1 20001201

parent continuation-of 09135988 19980817 US PATENTED

child 09729133 A1 20001201

parent continuation-in-part-of 08757046 19961125 US PATENTED

child 09729133 A1 20001201

parent continuation-in-part-of 08597274 19960206 US PATENTED

non-provisional-of-provisional 60079624 19980327 US

non-provisional-of-provisional 60089367 19980615 US

RELATED APPLICATIONS

[0001] This applicaiton is a continuation of U.S. application Ser. No. 09/444,762 to Bruce Bryan, filed Nov. 22, 1999, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also continuation of U.S. application Ser. No. 09/135,988 to Bruce Bryan, filed Aug. 17, 1998, now U.S. Pat. No. 6,152,358, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also continuation-in-part of U.S. application Ser. No. 08/757,046 to Bruce Bryan, filed Nov. 25, 1996, now U.S. Pat. No. 5,876,995, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also a continuation-in-part of U.S. application Ser. No. 08/597,274, now allowed, to Bruce Bryan, filed Feb. 6, 1996, entitled "BIOLUMINESCENT NOVELTY ITEMS".

[0002] U.S. application Ser. No. 09/444,762 is a continuation of U.S. application Ser. No. 09/135,988, which is a continuation-in-part of U.S. application Ser. No. 08/757,046, which is a continuation-in-part of U.S. application Ser. No. 08/597,274. The subject matter of each of U.S. application Ser. Nos. 09/135,988, 08/597,274 and 08/757,046 is herein incorporated in its entirety by reference thereto. This application is also

related to provisional application serial numbers 60/079,624 and 60/089,367. The disclosures of each of the above noted patents, applications and provisional applications is incorporated herein by reference thereto.

PGPUB-DOCUMENT-NUMBER: 20030059798

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030059798 A1

TITLE: Apparatus and method for detecting and identifying infectious agents

PUBLICATION-DATE: March 27, 2003

US-CL-CURRENT: 435/6

APPL-NO: 10/ 126798

DATE FILED: April 19, 2002

RELATED-US-APPL-DATA:

child 10126798 A1 20020419

parent division-of 08990103 19971212 US GRANTED

parent-patent 6458547 US

non-provisional-of-provisional 60037675 19970211 US

non-provisional-of-provisional 60033745 19961212 US

RELATED APPLICATIONS

[0001] This application claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional appplication Serial No. 60/037,675, filed Feb. 11, 1997 and to U.S. Provisional application Serial No. 60/033,745, filed Dec. 12, 1996.

[0002] Certain subject matter in this application is related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS" (B), and to U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES" and to U.S. Provisional application Serial No. 60/023,374, filed Aug. 8, 1996, entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES", and also to published International PCT application No. WO _____.

[0003] The subject matter of each of the above noted U.S. applications, provisional applications and international application is herein incorporated by reference in its entirety.

PGPUB-DOCUMENT-NUMBER: 20030055511

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030055511 A1

TITLE: Shaped particle comprised of bone material and method of making the particle

PUBLICATION-DATE: March 20, 2003

US-CL-CURRENT: 623/23.5, 623/16.11 , 623/23.63 , 623/919

APPL-NO: 10/ 099616

DATE FILED: March 15, 2002

RELATED-US-APPL-DATA:

child 10099616 A1 20020315

parent continuation-in-part-of 09517981 20000303 US PENDING

child 10099616 A1 20020315

parent continuation-in-part-of 09792681 20010223 US PENDING

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application is a Continuation-in-Part Application of U.S. patent application Ser. No. 09/517,981 filed Mar. 3, 2000 and a Continuation-in-Part Application of U.S. patent application Ser. No. 09/792,681 filed Feb. 23, 2001, both of which are incorporated by reference herein in their entirety.

US-PAT-NO: 6682899

DOCUMENT-IDENTIFIER: US 6682899 B2

TITLE: Apparatus and method for detecting and identifying infectious agents

DATE-ISSUED: January 27, 2004

US-CL-CURRENT: 435/7.1, 356/215 , 356/222 , 356/317 , 422/57 , 422/58 , 422/68.1 , 422/82.05 , 422/82.08 , 427/162 , 427/167 , 427/8 , 435/283.1 , 435/288.7 , 435/4 , 435/6 , 435/7.9 , 435/7.92 , 435/808 , 435/973 , 435/975 , 436/164 , 436/172 , 436/518 , 436/524 , 436/527 , 436/805

APPL-NO: 10/ 126777

DATE FILED: April 19, 2002

PARENT-CASE:

RELATED APPLICATIONS

This application is a divisional of application Ser. No. 08/990,103 filed Dec. 12, 1997 now U.S. Pat. No. 6,458,547. This application claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional application Ser. No. 60/037,675, filed Feb. 11, 1997 and to U.S. Provisional application Ser. No. 60/033,745, filed Dec. 12, 1996.

Certain subject matter in this application is related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS" (B), and to U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES" and to U.S. Provisional application Serial No. 60/023,374, filed Aug. 8, 1996, entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES", and also to published International PCT application No. WO 97/29,319.

The subject matter of each of the above noted U.S. applications, provisional applications and International application is herein incorporated by reference in its entirety.

US-PAT-NO: 6649357

DOCUMENT-IDENTIFIER: US 6649357 B2

TITLE: Apparatus and method for detecting and identifying infectious agents

DATE-ISSUED: November 18, 2003

US-CL-CURRENT: 435/7.1, 356/215 , 356/222 , 356/317 , 422/57 , 422/58 , 422/68.1 , 422/82.05 , 422/82.08 , 435/288.7 , 435/6 , 435/7.9 , 435/808 , 435/973 , 435/975 , 436/164 , 436/172 , 436/518 , 436/524 , 436/527 , 436/532 , 436/805

APPL-NO: 10/ 126798

DATE FILED: April 19, 2002

PARENT-CASE:

RELATED APPLICATIONS

This application is a divisional of application Ser. No. 08/990,103 filed Dec. 12, 1997 now U.S. Pat. No. 6,458,547. This application claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional application Serial No. 60/037,675, filed Feb. 11, 1997 and to U.S. Provisional application Serial No. 60/033,745, filed Dec. 12, 1996.

Certain subject matter in this application is related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS" (B), and to U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES" and to U.S. Provisional application Serial No. 60/023,374, filed Aug. 8, 1996, entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES", and also to published International PCT application No. WO _____.

The subject matter of each of the above noted U.S. applications, provisional applications and international application is herein incorporated by reference in its entirety.

US-PAT-NO: 6649356

DOCUMENT-IDENTIFIER: US 6649356 B2

TITLE: Apparatus and method for detecting and identifying infectious agents

DATE-ISSUED: November 18, 2003

US-CL-CURRENT: 435/7.1, 356/215 , 356/222 , 356/317 , 422/57 , 422/58 , 422/68.1 , 422/82.05 , 422/82.08 , 435/288.7 , 435/6 , 435/7.9 , 435/808 , 435/973 , 435/975 , 436/122 , 436/164 , 436/518 , 436/524 , 436/527 , 436/532 , 436/805

APPL-NO: 10/ 126139

DATE FILED: April 19, 2002

PARENT-CASE:

RELATED APPLICATIONS

This application is a divisional of application Ser. No. 08/990,103 filed Dec. 12, 1997 now U.S. Pat. No. 6,458,547.This application claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional application Serial No. 60/037,675, filed Feb. 11, 1997 and to U.S. Provisional application Serial No. 60/033,745, filed Dec. 12, 1996.

Certain subject matter in this application is related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS" (B), and to U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES" and to U.S. Provisional application Ser. No. 60/023,374, filed Aug. 8, 1996, entitled "DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES", and also to published International PCT application No. WO 97/29,319.

The subject matter of each of the above noted U.S. applications, provisional applications and International application is herein incorporated by reference in its entirety.

US-PAT-NO: 6630153

DOCUMENT-IDENTIFIER: US 6630153 B2

TITLE: Manufacture of bone graft substitutes

DATE-ISSUED: October 7, 2003

US-CL-CURRENT: 424/422, 424/423 , 424/426 , 424/484 , 424/501

APPL-NO: 09/ 792681

DATE FILED: February 23, 2001

US-PAT-NO: 6596257

DOCUMENT-IDENTIFIER: US 6596257 B2

TITLE: Detection and visualization of neoplastic tissues and other tissues

DATE-ISSUED: July 22, 2003

US-CL-CURRENT: 424/9.1, 424/9.6

APPL-NO: 09/ 746485

DATE FILED: December 22, 2000

PARENT-CASE:

CROSS REFERENCE TO RELATED APPLICATION

This application is a continuation-in-part of U.S. Ser. No. 08/908,909 filed Aug. 8, 1997 to Bruce Bryan, entitled "DETECTION AND VISUALIZATION OF NEOPLASTIC TISSUES AND OTHER TISSUES" now U.S. Pat. No. 6,416,960. This application and U.S. application Ser. No. 08/908,909 claim the benefit of priority under 35 U.S.C. .sctn.119(e) to U.S. provisional application Ser. No. 60/023,374 to Bruce Bryan, filed Aug. 8, 1996, and entitled DETECTION AND VISUALIZATION OF NEOPLASMS AND OTHER TISSUES.

RELATED APPLICATIONS

Subject matter in this application is related to subject matter in allowed U.S. application Ser. No. 08/597,274 to Bruce Bryan, filed Feb. 6, 1996, entitled "BIOLUMINESCENT NOVELTY ITEMS", and U.S. application Ser. No. 08/757,046 to Bruce Bryan, filed Nov. 25, 1996, now U.S. Pat. No. 5,876,995, entitled "BIOLUMINESCENT NOVELTY ITEMS". The subject matter of each of U.S. application Ser. No. 08/597,274 and U.S. application Ser. No. 08/757,046, and U.S. provisional application Serial No. 60/023,374 is herein incorporated in its entirety by reference thereto.